



## Clinical trial results:

**A randomized, double-blind, placebo-controlled, event-driven trial of quarterly subcutaneous canakinumab in the prevention of recurrent cardiovascular events among stable post-myocardial infarction patients with elevated hsCRP**

### Summary

|                          |   |
|--------------------------|---|
| EudraCT number           | 2010-022970-14  |
| Trial protocol           | SK DE HU SE PL LV LT AT GB EE GR IS BE NO CZ IT BG SI |
| Global end of trial date | 14 April 2019   |

### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 01 January 2020 |
| First version publication date | 01 January 2020 |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CACZ885M2301 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01327846 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharma, AG   |
| Sponsor organisation address | CH-4002, Basel, Switzerland,  |
| Public contact               | Clinical Disclosure Office, Novartis Pharama, AG, 41 613241111, Novartis.email@novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma, AG, 41 613241111, Novartis.email@novartis.com  |

Notes:

### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 14 April 2019 |
| Is this the analysis of the primary completion data? | No            |

|                                  |               |
|----------------------------------|---------------|
| Global end of trial reached?     | Yes           |
| Global end of trial date         | 14 April 2019 |
| Was the trial ended prematurely? | Yes           |

Notes:

## General information about the trial

Main objective of the trial:

Core phase: The primary objective of this study was to demonstrate the superiority of at least one dose of canakinumab compared to placebo in reducing the risk of recurrent major cardiovascular events (cardiovascular death, non-fatal MI and non-fatal stroke) in a population of clinically stable patients with prior MI with elevated hsCRP receiving standard of care. Extension phase: The purpose of the Extension phase was to obtain further follow-up information on long-term safety on continued exposure to canakinumab in trial participants.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 11 April 2011 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Argentina: 375      |
| Country: Number of subjects enrolled | Australia: 86       |
| Country: Number of subjects enrolled | Austria: 58         |
| Country: Number of subjects enrolled | Belgium: 94         |
| Country: Number of subjects enrolled | Brazil: 719         |
| Country: Number of subjects enrolled | Bulgaria: 209       |
| Country: Number of subjects enrolled | Canada: 398         |
| Country: Number of subjects enrolled | China: 126          |
| Country: Number of subjects enrolled | Colombia: 183       |
| Country: Number of subjects enrolled | Croatia: 36         |
| Country: Number of subjects enrolled | Czech Republic: 382 |
| Country: Number of subjects enrolled | Estonia: 70         |
| Country: Number of subjects enrolled | Germany: 643        |
| Country: Number of subjects enrolled | Greece: 64          |
| Country: Number of subjects enrolled | Guatemala: 81       |
| Country: Number of subjects enrolled | Hungary: 328        |
| Country: Number of subjects enrolled | Iceland: 119        |

|                                      |  |
|--------------------------------------|--|
| Country: Number of subjects enrolled | India: 592                                 |
| Country: Number of subjects enrolled | Italy: 231                                 |
| Country: Number of subjects enrolled | Japan: 235                                 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 62 |
| Country: Number of subjects enrolled | Latvia: 43                                 |
| Country: Number of subjects enrolled | Lithuania: 121                             |
| Country: Number of subjects enrolled | Mexico: 61                                 |
| Country: Number of subjects enrolled | Netherlands: 623                           |
| Country: Number of subjects enrolled | Norway: 133                                |
| Country: Number of subjects enrolled | Peru: 11                                   |
| Country: Number of subjects enrolled | Poland: 142                                |
| Country: Number of subjects enrolled | Romania: 293                               |
| Country: Number of subjects enrolled | Russian Federation: 315                    |
| Country: Number of subjects enrolled | Serbia: 45                                 |
| Country: Number of subjects enrolled | Slovakia: 401                              |
| Country: Number of subjects enrolled | Slovenia: 78                               |
| Country: Number of subjects enrolled | South Africa: 63                           |
| Country: Number of subjects enrolled | Sweden: 202                                |
| Country: Number of subjects enrolled | Taiwan: 106                                |
| Country: Number of subjects enrolled | Turkey: 26                                 |
| Country: Number of subjects enrolled | United Kingdom: 290                        |
| Country: Number of subjects enrolled | United States: 2017                        |
| Worldwide total number of subjects   | 10061                                      |
| EEA total number of subjects         | 4560                                       |

Notes:

### Subjects enrolled per age group

|   |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 6291 |
| From 65 to 84 years                       | 3717 |
| 85 years and over                         | 53   |

## Subject disposition

### Recruitment

Recruitment details:

10066 patients enrolled in Core phase (4 randomized groups); 5 patients enrolled in safety set were not included in efficacy set. 5777 patients continued in Extension phase (539 only washout period, 5238 in treatment period(s)). The Core phase completed as planned; the Extension phase was terminated. Sub-studies terminated prior to data collection.

### Pre-assignment

Screening details:

A total of 17482 patients were screened, and 10102 patients completed the screening phase. A total of 6430 patients did not complete the screening phase due to screen failure.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Core Phase  |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                                       |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Group I |

Arm description:

Core phase: Blinded Canakinumab 300 mg quarterly subcutaneous + standard of care (SoC) therapy  
Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Canakinumab                                  |
| Investigational medicinal product code | ACZ885                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

300 mg quarterly sc (2x canakinumab 150 mg in 1mL solution)

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Group II |
|------------------|----------|

Arm description:

Core phase: Blinded Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy  
Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Canakinumab                                  |
| Investigational medicinal product code | ACZ855                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

150 mg in 1 mL solution quarterly sc

|                  |           |
|------------------|-----------|
| <b>Arm title</b> | Group III |
|------------------|-----------|

Arm description:

Core phase: Blinded Canakinumab 50 mg quarterly subcutaneous + standard of care (SoC) therapy  
Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Canakinumab                                  |
| Investigational medicinal product code | ACZ855                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

50 mg in 0.5 mL solution quarterly sc

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Group IV |
|------------------|----------|

Arm description:

Core phase: Blinded matching placebo quarterly subcutaneous + standard of care (SoC) therapy

Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|  |  |
|--|--|
| Arm type                               | Placebo                                      |
| Investigational medicinal product name | Canakinumab matching placebo                 |
| Investigational medicinal product code | Canakinumab matching placebo                 |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

50 mg matching placebo quarterly sc and/or 150 mg quarterly sc matching placebo

| <b>Number of subjects in period 1</b>    | Group I | Group II | Group III |
|--|---------|----------|-----------|
| Started                                  | 2263    | 2284     | 2170      |
| Completed                                | 2235    | 2252     | 2144      |
| Not completed                            | 28      | 32       | 26        |
| Subject decision (vital status: missing) | 1       | 2        | 2         |
| Subject decision (vital stat: alive)     | 23      | 24       | 13        |
| Subject decision (vital stat: unkn)      | -       | -        | 3         |
| Lost to follow-up                        | 3       | 3        | 4         |
| Subject decision (vital stat: dead)      | 1       | 3        | 4         |

| <b>Number of subjects in period 1</b>    | Group IV |
|--|----------|
| Started                                  | 3344     |
| Completed                                | 3311     |
| Not completed                            | 33       |
| Subject decision (vital status: missing) | 1        |
| Subject decision (vital stat: alive)     | 20       |
| Subject decision (vital stat: unkn)      | 3        |
| Lost to follow-up                        | 5        |
| Subject decision (vital stat: dead)      | 4        |

|  |  |
|--|--|
| <b>Period 2</b>  |  |
| Period 2 title   | Extension Phase                              |
| Is this the baseline period?   | No   |
| Allocation method  | Non-randomised - controlled                  |
| Blinding used  | Not blinded                                  |
| <b>Arms</b>  |  |
| Are arms mutually exclusive?   | Yes  |
| <b>Arm title</b>   | Group I                                      |
| Arm description:   |  |
| Core phase: Blinded Canakinumab 300 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |  |
| Arm type   | Experimental                                 |
| Investigational medicinal product name   | Canakinumab                                  |
| Investigational medicinal product code   | ACZ885                                       |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled syringe |
| Routes of administration   | Subcutaneous use                             |
| Dosage and administration details:   |  |
| 150 mg in 1 mL solution quarterly sc   |  |
| <b>Arm title</b>   | Group II                                     |
| Arm description:   |  |
| Core phase: Blinded Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |  |
| Arm type   | Experimental                                 |
| Investigational medicinal product name   | Canakinumab                                  |
| Investigational medicinal product code   | ACZ855                                       |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled syringe |
| Routes of administration   | Subcutaneous use                             |
| Dosage and administration details:   |  |
| 150 mg in 1 mL solution quarterly sc   |  |
| <b>Arm title</b>   | Group III                                    |
| Arm description:   |  |
| Core phase: Blinded Canakinumab 50 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy  |  |
| Arm type   | Experimental                                 |
| Investigational medicinal product name   | Canakinumab                                  |
| Investigational medicinal product code   | ACZ855                                       |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection in pre-filled syringe |
| Routes of administration   | Subcutaneous use                             |
| Dosage and administration details:   |  |
| 150 mg in 1 mL solution quarterly sc   |  |
| <b>Arm title</b>   | Group IV                                     |

Arm description:

Core phase: Blinded matching placebo quarterly subcutaneous + standard of care (SoC) therapy  
 Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | Canakinumab                                  |
| Investigational medicinal product code | ACZ855                                       |
| Other name                             |  |
| Pharmaceutical forms                   | Solution for injection in pre-filled syringe |
| Routes of administration               | Subcutaneous use                             |

Dosage and administration details:

150 mg in 1 mL solution quarterly sc

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Group I            | Group II          | Group III          |
|---|--------------------|-------------------|--------------------|
| Started   | 1267               | 1287              | 1279               |
| Stopped/discontinued study at washout               | 127 <sup>[2]</sup> | 97 <sup>[3]</sup> | 137 <sup>[4]</sup> |
| Completed treatment period                          | 41 <sup>[5]</sup>  | 45 <sup>[6]</sup> | 49 <sup>[7]</sup>  |
| Details missing                                     | 0 <sup>[8]</sup>   | 1 <sup>[9]</sup>  | 1 <sup>[10]</sup>  |
| Completed   | 168                | 143               | 187                |
| Not completed                                       | 1099               | 1144              | 1092               |
| Consent withdrawn by subject                        | 20                 | 13                | 19                 |
| Technical Problems                                  | 2                  | 4                 | 2                  |
| Study terminated by sponsor                         | 1073               | 1124              | 1067               |
| Lost to follow-up                                   | 4                  | 3                 | 4                  |

| <b>Number of subjects in period 2<sup>[1]</sup></b> | Group IV            |
|---|---------------------|
| Started   | 1944                |
| Stopped/discontinued study at washout               | 178 <sup>[11]</sup> |
| Completed treatment period                          | 60 <sup>[12]</sup>  |
| Details missing                                     | 0 <sup>[13]</sup>   |
| Completed   | 238                 |
| Not completed                                       | 1706                |
| Consent withdrawn by subject                        | 37                  |
| Technical Problems                                  | 2                   |
| Study terminated by sponsor                         | 1660                |
| Lost to follow-up                                   | 7                   |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.

[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This study was conducted in 2 phases: A Core phase and an extension phase.



## Baseline characteristics

### Reporting groups

|  |           |
|--|-----------|
| Reporting group title  | Group I   |
| Reporting group description:   |           |
| Core phase: Blinded Canakinumab 300 mg quarterly subcutaneous + standard of care (SoC) therapy                     |           |
| Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |
| Reporting group title  | Group II  |
| Reporting group description:   |           |
| Core phase: Blinded Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy                     |           |
| Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |
| Reporting group title  | Group III |
| Reporting group description:   |           |
| Core phase: Blinded Canakinumab 50 mg quarterly subcutaneous + standard of care (SoC) therapy                      |           |
| Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |
| Reporting group title  | Group IV  |
| Reporting group description:   |           |
| Core phase: Blinded matching placebo quarterly subcutaneous + standard of care (SoC) therapy                       |           |
| Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |

| Reporting group values     | Group I | Group II | Group III |
|----------------------------|---------|----------|-----------|
| Number of subjects         | 2263    | 2284     | 2170      |
| Age, Customized            |         |          |           |
| Units: Subjects            |         |          |           |
| < 65                       | 1424    | 1428     | 1350      |
| 65 < 85                    | 828     | 838      | 807       |
| >85                        | 11      | 18       | 13        |
| Sex: Female, Male          |         |          |           |
| Units: Subjects            |         |          |           |
| Female                     | 606     | 575      | 541       |
| Male                       | 1657    | 1709     | 1629      |
| Race/Ethnicity, Customized |         |          |           |
| Units: Subjects            |         |          |           |
| Caucasian                  | 1804    | 1808     | 1772      |
| Black                      | 84      | 67       | 61        |
| Asian                      | 265     | 278      | 232       |
| Native American            | 47      | 49       | 41        |
| Pacific Islander           | 0       | 0        | 1         |
| Unknown                    | 3       | 3        | 1         |
| Other                      | 60      | 79       | 62        |

| Reporting group values | Group IV | Total |  |
|------------------------|----------|-------|--|
| Number of subjects     | 3344     | 10061 |  |
| Age, Customized        |          |       |  |
| Units: Subjects        |          |       |  |
| < 65                   | 2089     | 6291  |  |
| 65 < 85                | 1244     | 3717  |  |

|     |    |    |  |
|-----|----|----|--|
| >85 | 11 | 53 |  |
|-----|----|----|--|

|   |      |      |  |
|---|------|------|--|
| Sex: Female, Male<br>Units: Subjects          |      |      |  |
| Female  | 865  | 2587 |  |
| Male  | 2479 | 7474 |  |
| Race/Ethnicity, Customized<br>Units: Subjects |      |      |  |
| Caucasian                                     | 2652 | 8036 |  |
| Black   | 106  | 318  |  |
| Asian   | 388  | 1163 |  |
| Native American                               | 82   | 219  |  |
| Pacific Islander                              | 1    | 2    |  |
| Unknown                                       | 3    | 10   |  |
| Other   | 112  | 313  |  |

## End points

### End points reporting groups

|  |           |
|--|-----------|
| Reporting group title  | Group I   |
| Reporting group description:<br>Core phase: Blinded Canakinumab 300 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |
| Reporting group title  | Group II  |
| Reporting group description:<br>Core phase: Blinded Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |
| Reporting group title  | Group III |
| Reporting group description:<br>Core phase: Blinded Canakinumab 50 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy  |           |
| Reporting group title  | Group IV  |
| Reporting group description:<br>Core phase: Blinded matching placebo quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy   |           |
| Reporting group title  | Group I   |
| Reporting group description:<br>Core phase: Blinded Canakinumab 300 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |
| Reporting group title  | Group II  |
| Reporting group description:<br>Core phase: Blinded Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy |           |
| Reporting group title  | Group III |
| Reporting group description:<br>Core phase: Blinded Canakinumab 50 mg quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy  |           |
| Reporting group title  | Group IV  |
| Reporting group description:<br>Core phase: Blinded matching placebo quarterly subcutaneous + standard of care (SoC) therapy<br>Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy   |           |

### Primary: Analysis of Core phase First CEC Confirmed Major Adverse Cardiovascular Events (MACE) and its components

|  |  |
|--|--|
| End point title  | Analysis of Core phase First CEC Confirmed Major Adverse Cardiovascular Events (MACE) and its components |
| End point description:<br>Time to occurrence of CEC (Cardiovascular clinical events adjudication committee) confirmed MACE, which was a composite endpoint consisting of CEC confirmed CV death, CEC confirmed non-fatal MI, or CEC confirmed non-fatal stroke. Patients with the CEC adjudicated reason for death of "Unknown" were counted as CV (cardiovascular) death. |  |
| End point type   | Primary  |

End point timeframe:

From randomization to end of treatment plus 30 days, up to approximately 6 years

| End point values             | Group I         | Group II        | Group III       | Group IV        |
|------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type           | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed  | 2263            | 2284            | 2170            | 3344            |
| Units: Participants          |                 |                 |                 |                 |
| MACE                         | 322             | 320             | 313             | 535             |
| CV death                     | 151             | 144             | 137             | 235             |
| MI (fatal and non-fatal)     | 174             | 159             | 169             | 292             |
| MI (non-fatal)               | 171             | 158             | 168             | 291             |
| Stroke (fatal and non-fatal) | 51              | 63              | 58              | 92              |
| Stroke (non-fatal)           | 51              | 63              | 58              | 91              |

## Statistical analyses

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>   | Primary Analysis [MACE] |
| Statistical analysis description:   |                         |
| H11: The hazard rate of first adjudication committee confirmed MACE in the canakinumab 300 mg dose group is greater than or equal to the hazard rate of the placebo group |                         |
| Comparison groups   | Group I v Group IV      |
| Number of subjects included in analysis   | 5607                    |
| Analysis specification  | Pre-specified           |
| Analysis type   |                         |
| P-value   | = 0.0648 <sup>[1]</sup> |
| Method  | Logrank                 |
| Parameter estimate  | Cox proportional hazard |
| Point estimate  | 0.86                    |
| Confidence interval   |                         |
| level   | 95 %                    |
| sides   | 2-sided                 |
| lower limit   | 0.75                    |
| upper limit   | 0.99                    |

Notes:

[1] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>   | Primary Analysis [MACE] |
| Statistical analysis description:   |                         |
| H21: The hazard rate of first adjudication committee confirmed MACE in the canakinumab 150 mg dose group is greater than or equal to the hazard rate of the placebo group |                         |
| Comparison groups   | Group II v Group IV     |

|   |                         |
|---|-------------------------|
| Number of subjects included in analysis | 5628                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.0241 <sup>[2]</sup> |
| Method                                  | Logrank                 |
| Parameter estimate                      | Cox proportional hazard |
| Point estimate                          | 0.85                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.74                    |
| upper limit                             | 0.98                    |

Notes:

[2] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>   | Primary Analysis [MACE] |
| Statistical analysis description:   |                         |
| H31: The hazard rate of first adjudication committee confirmed MACE in the canakinumab 50 mg dose group is greater than or equal to the hazard rate of the placebo group. |                         |
| Comparison groups   | Group III v Group IV    |
| Number of subjects included in analysis   | 5514                    |
| Analysis specification  | Pre-specified           |
| Analysis type   |                         |
| P-value   | = 0.1895 <sup>[3]</sup> |
| Method  | Logrank                 |
| Parameter estimate  | Cox proportional hazard |
| Point estimate  | 0.93                    |
| Confidence interval   |                         |
| level   | 95 %                    |
| sides   | 2-sided                 |
| lower limit   | 0.8                     |
| upper limit   | 1.07                    |

Notes:

[3] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | Primary Analysis [CV Death] |
| Comparison groups                       | Group I v Group IV          |
| Number of subjects included in analysis | 5607                        |
| Analysis specification                  | Pre-specified               |
| Analysis type                           |                             |
| P-value                                 | = 0.572 <sup>[4]</sup>      |
| Method                                  | Regression, Cox             |
| Parameter estimate                      | Hazard ratio (HR)           |
| Point estimate                          | 0.94                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.77                        |
| upper limit                             | 1.16                        |

Notes:

[4] - 2-sided unadjusted p-value

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | Primary Analysis [CV Death] |
| Comparison groups                       | Group II v Group IV         |
| Number of subjects included in analysis | 5628                        |
| Analysis specification                  | Pre-specified               |
| Analysis type                           |                             |
| P-value                                 | = 0.296 <sup>[5]</sup>      |
| Method                                  | Regression, Cox             |
| Parameter estimate                      | Hazard ratio (HR)           |
| Point estimate                          | 0.9                         |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.73                        |
| upper limit                             | 1.1                         |

Notes:

[5] - 2-sided unadjusted p-value

|   |                             |
|---|-----------------------------|
| <b>Statistical analysis title</b>       | Primary Analysis [CV Death] |
| Comparison groups                       | Group III v Group IV        |
| Number of subjects included in analysis | 5514                        |
| Analysis specification                  | Pre-specified               |
| Analysis type                           |                             |
| P-value                                 | = 0.369 <sup>[6]</sup>      |
| Method                                  | Regression, Cox             |
| Parameter estimate                      | Hazard ratio (HR)           |
| Point estimate                          | 0.91                        |
| Confidence interval                     |                             |
| level                                   | 95 %                        |
| sides                                   | 2-sided                     |
| lower limit                             | 0.73                        |
| upper limit                             | 1.12                        |

Notes:

[6] - 2-sided unadjusted p-value

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Primary Analysis [MI (Fatal and Non-Fatal)] |
| Comparison groups                       | Group I v Group IV                          |
| Number of subjects included in analysis | 5607  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           |   |
| P-value                                 | = 0.067 <sup>[7]</sup>                      |
| Method                                  | Regression, Cox                             |
| Parameter estimate                      | Hazard ratio (HR)                           |
| Point estimate                          | 0.84  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.69    |
| upper limit         | 1.01    |

Notes:

[7] - 2-sided unadjusted p-value

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Primary Analysis [MI (Fatal and Non-Fatal)] |
| Comparison groups                       | Group II v Group IV                         |
| Number of subjects included in analysis | 5628  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           |   |
| P-value                                 | = 0.006 <sup>[8]</sup>                      |
| Method                                  | Regression, Cox                             |
| Parameter estimate                      | Hazard ratio (HR)                           |
| Point estimate                          | 0.76  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                     |
| lower limit                             | 0.63  |
| upper limit                             | 0.92  |

Notes:

[8] - 2-sided unadjusted p-value

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Primary Analysis [MI (Fatal and Non-Fatal)] |
| Comparison groups                       | Group III v Group IV                        |
| Number of subjects included in analysis | 5514  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           |   |
| P-value                                 | = 0.542 <sup>[9]</sup>                      |
| Method                                  | Regression, Cox                             |
| Parameter estimate                      | Hazard ratio (HR)                           |
| Point estimate                          | 0.94  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                     |
| lower limit                             | 0.78  |
| upper limit                             | 1.14  |

Notes:

[9] - 2-sided unadjusted p-value

|                                   |                                   |
|-----------------------------------|-----------------------------------|
| <b>Statistical analysis title</b> | Primary Analysis [MI (Non-Fatal)] |
| Comparison groups                 | Group I v Group IV                |

|   |                   |
|---|-------------------|
| Number of subjects included in analysis | 5607              |
| Analysis specification                  | Pre-specified     |
| Analysis type                           |                   |
| Parameter estimate                      | Hazard ratio (HR) |
| Point estimate                          | 0.83              |
| Confidence interval                     |                   |
| level                                   | 95 %              |
| sides                                   | 2-sided           |
| lower limit                             | 0.68              |
| upper limit                             | 1                 |

|   |                                   |
|---|-----------------------------------|
| <b>Statistical analysis title</b>       | Primary Analysis [MI (Non-Fatal)] |
| Comparison groups                       | Group II v Group IV               |
| Number of subjects included in analysis | 5628                              |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Hazard ratio (HR)                 |
| Point estimate                          | 0.76                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 0.62                              |
| upper limit                             | 0.92                              |

|   |                                   |
|---|-----------------------------------|
| <b>Statistical analysis title</b>       | Primary Analysis [MI (Non-Fatal)] |
| Comparison groups                       | Group III v Group IV              |
| Number of subjects included in analysis | 5514                              |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           |                                   |
| Parameter estimate                      | Hazard ratio (HR)                 |
| Point estimate                          | 0.94                              |
| Confidence interval                     |                                   |
| level                                   | 95 %                              |
| sides                                   | 2-sided                           |
| lower limit                             | 0.78                              |
| upper limit                             | 1.14                              |

|                                   |   |
|-----------------------------------|---|
| <b>Statistical analysis title</b> | Primary Analysis [Stroke (Fatal and Non-Fatal)] |
| Comparison groups                 | Group I v Group IV                              |



|   |                        |
|---|------------------------|
| Number of subjects included in analysis | 5607                   |
| Analysis specification                  | Pre-specified          |
| Analysis type                           |                        |
| P-value                                 | = 0.19 <sup>[10]</sup> |
| Method                                  | Regression, Cox        |
| Parameter estimate                      | Hazard ratio (HR)      |
| Point estimate                          | 0.8                    |
| Confidence interval                     |                        |
| level                                   | 95 %                   |
| sides                                   | 2-sided                |
| lower limit                             | 0.56                   |
| upper limit                             | 1.12                   |

Notes:

[10] - 2-sided unadjusted p-value

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Primary Analysis [Stroke (Fatal and Non-Fatal)] |
| Comparison groups                       | Group II v Group IV                             |
| Number of subjects included in analysis | 5628  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           |   |
| P-value                                 | = 0.912 <sup>[11]</sup>                         |
| Method                                  | Regression, Cox                                 |
| Parameter estimate                      | Hazard ratio (HR)                               |
| Point estimate                          | 0.98  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 0.71  |
| upper limit                             | 1.35  |

Notes:

[11] - 2-sided unadjusted p-value

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Primary Analysis [Stroke (Fatal and Non-Fatal)] |
| Comparison groups                       | Group III v Group IV                            |
| Number of subjects included in analysis | 5514  |
| Analysis specification                  | Pre-specified                                   |
| Analysis type                           |   |
| P-value                                 | = 0.871 <sup>[12]</sup>                         |
| Method                                  | Regression, Cox                                 |
| Parameter estimate                      | Hazard ratio (HR)                               |
| Point estimate                          | 1.03  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided   |
| lower limit                             | 0.74  |
| upper limit                             | 1.43  |

Notes:

[12] - 2-sided unadjusted p-value

|                                   |                                       |
|-----------------------------------|---------------------------------------|
| <b>Statistical analysis title</b> | Primary Analysis [Stroke (Non-Fatal)] |
|-----------------------------------|---------------------------------------|

|   |                    |
|---|--------------------|
| Comparison groups                       | Group I v Group IV |
| Number of subjects included in analysis | 5607               |
| Analysis specification                  | Pre-specified      |
| Analysis type                           |                    |
| Parameter estimate                      | Hazard ratio (HR)  |
| Point estimate                          | 0.8                |
| Confidence interval                     |                    |
| level                                   | 95 %               |
| sides                                   | 2-sided            |
| lower limit                             | 0.57               |
| upper limit                             | 1.13               |

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Primary Analysis [Stroke (Non-Fatal)] |
| Comparison groups                       | Group II v Group IV                   |
| Number of subjects included in analysis | 5628                                  |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           |                                       |
| Parameter estimate                      | Hazard ratio (HR)                     |
| Point estimate                          | 0.99                                  |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 0.72                                  |
| upper limit                             | 1.37                                  |

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Primary Analysis [Stroke (Non-Fatal)] |
| Comparison groups                       | Group III v Group IV                  |
| Number of subjects included in analysis | 5514                                  |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           |                                       |
| Parameter estimate                      | Hazard ratio (HR)                     |
| Point estimate                          | 1.04                                  |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 0.75                                  |
| upper limit                             | 1.45                                  |

**Primary: Substudy 1 (Core phase): Change from baseline in carotid plaque burden in the bifurcation region of the index carotid artery**

|                 |  |
|-----------------|--|
| End point title | Substudy 1 (Core phase): Change from baseline in carotid plaque burden in the bifurcation region of the index carotid artery <sup>[13]</sup> |
|-----------------|--|

End point description:

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| 24 months            |         |

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Substudy 1 was cancelled; no statistical analyses was performed.

| End point values             | Group I           | Group II          | Group III         | Group IV          |
|------------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type           | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed  | 0 <sup>[14]</sup> | 0 <sup>[15]</sup> | 0 <sup>[16]</sup> | 0 <sup>[17]</sup> |
| Units: carotid plaque burden |                   |                   |                   |                   |

Notes:

[14] - Analysis not performed

[15] - Analysis not performed

[16] - Analysis not performed

[17] - Analysis not performed

## Statistical analyses

No statistical analyses for this end point

**Primary: Substudy 2 (Core phase): Change from baseline of the insulin secretion rate (ISR) relative to glucose 0-30 min defined as  $\Phi 30 = \text{AUCISR 0-30} / \text{AUCGluc 0-30}$  averaged across the year 3, 4, 5 visits**

|                 |  |
|-----------------|--|
| End point title | Substudy 2 (Core phase): Change from baseline of the insulin secretion rate (ISR) relative to glucose 0-30 min defined as $\Phi 30 = \text{AUCISR 0-30} / \text{AUCGluc 0-30}$ averaged across the year 3, 4, 5 visits <sup>[18]</sup> |
|-----------------|--|

End point description:

|  |         |
|--|---------|
| End point type                                 | Primary |
| End point timeframe:                           |         |
| From randomization up to approximately 6 years |         |

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Substudy 2 was cancelled; no statistical analyses was performed.

| End point values                | Group I           | Group II          | Group III         | Group IV          |
|---------------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type              | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed     | 0 <sup>[19]</sup> | 0 <sup>[20]</sup> | 0 <sup>[21]</sup> | 0 <sup>[22]</sup> |
| Units: change in ISR to glucose |                   |                   |                   |                   |

Notes:

[19] - Analysis not performed

[20] - Analysis not performed

[21] - Analysis not performed

[22] - Analysis not performed

## Statistical analyses

**Secondary: Patients with Core phase CEC confirmed CV death, non-fatal MI, non-fatal stroke, or hospitalization for unstable angina requiring unplanned revascularization**

|                 |   |
|-----------------|---|
| End point title | Patients with Core phase CEC confirmed CV death, non-fatal MI, non-fatal stroke, or hospitalization for unstable angina requiring unplanned revascularization |
|-----------------|---|

## End point description:

Occurrence of the composite cardiovascular endpoint consisting of cardiovascular death, non-fatal MI, non-fatal stroke or hospitalization for unstable angina requiring unplanned revascularization MACE includes CV death, non-fatal MI and non-fatal stroke. CEC = Clinical Endpoints Committee

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

## End point timeframe:

From randomization, to end of treatment plus 30 days, up to approximately 6 years

| End point values            | Group I         | Group II        | Group III       | Group IV        |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2263            | 2284            | 2170            | 3344            |
| Units: Participants         |                 |                 |                 |                 |
| MACE or unstable angina     | 348             | 352             | 344             | 601             |
| Unstable angina             | 34              | 38              | 38              | 85              |

**Statistical analyses**

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>       | Analysis [MACE or Unstable Angina] |
| Comparison groups                       | Group I v Group IV                 |
| Number of subjects included in analysis | 5607                               |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| P-value                                 | = 0.0648 <sup>[23]</sup>           |
| Method                                  | Logrank                            |
| Parameter estimate                      | Hazard ratio (HR)                  |
| Point estimate                          | 0.82                               |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.72                               |
| upper limit                             | 0.94                               |

## Notes:

[23] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|                                   |                                    |
|-----------------------------------|------------------------------------|
| <b>Statistical analysis title</b> | Analysis [MACE or Unstable Angina] |
| Comparison groups                 | Group II v Group IV                |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 5628                     |
| Analysis specification                  | Pre-specified            |
| Analysis type                           |                          |
| P-value                                 | = 0.0241 <sup>[24]</sup> |
| Method                                  | Logrank                  |
| Parameter estimate                      | Hazard ratio (HR)        |
| Point estimate                          | 0.83                     |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | 0.73                     |
| upper limit                             | 0.95                     |

Notes:

[24] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|   |                                    |
|---|------------------------------------|
| <b>Statistical analysis title</b>       | Analysis [MACE or Unstable Angina] |
| Comparison groups                       | Group III v Group IV               |
| Number of subjects included in analysis | 5514                               |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           |                                    |
| P-value                                 | = 0.1895 <sup>[25]</sup>           |
| Method                                  | Logrank                            |
| Parameter estimate                      | Hazard ratio (HR)                  |
| Point estimate                          | 0.9                                |
| Confidence interval                     |                                    |
| level                                   | 95 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | 0.79                               |
| upper limit                             | 1.03                               |

Notes:

[25] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|   |                            |
|---|----------------------------|
| <b>Statistical analysis title</b>       | Analysis [Unstable Angina] |
| Comparison groups                       | Group I v Group IV         |
| Number of subjects included in analysis | 5607                       |
| Analysis specification                  | Pre-specified              |
| Analysis type                           |                            |
| P-value                                 | = 0.007 <sup>[26]</sup>    |
| Method                                  | Regression, Cox            |
| Parameter estimate                      | Hazard ratio (HR)          |
| Point estimate                          | 0.58                       |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.39                       |
| upper limit                             | 0.86                       |

Notes:

[26] - 2-sided unadjusted p-value

|                                   |                            |
|-----------------------------------|----------------------------|
| <b>Statistical analysis title</b> | Analysis [Unstable Angina] |
|-----------------------------------|----------------------------|

|   |                         |
|---|-------------------------|
| Comparison groups                       | Group II v Group IV     |
| Number of subjects included in analysis | 5628                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.022 <sup>[27]</sup> |
| Method                                  | Regression, Cox         |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.64                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.44                    |
| upper limit                             | 0.94                    |

Notes:

[27] - 2-sided unadjusted p-value

|   |                            |
|---|----------------------------|
| <b>Statistical analysis title</b>       | Analysis [Unstable Angina] |
| Comparison groups                       | Group III v Group IV       |
| Number of subjects included in analysis | 5514                       |
| Analysis specification                  | Pre-specified              |
| Analysis type                           |                            |
| P-value                                 | = 0.086 <sup>[28]</sup>    |
| Method                                  | Regression, Cox            |
| Parameter estimate                      | Hazard ratio (HR)          |
| Point estimate                          | 0.71                       |
| Confidence interval                     |                            |
| level                                   | 95 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 0.48                       |
| upper limit                             | 1.05                       |

Notes:

[28] - 2-sided unadjusted p-value

### **Secondary: Patients with Core phase new onset type 2 diabetes among patients with pre-diabetes at randomization**

|   |  |
|---|--|
| End point title   | Patients with Core phase new onset type 2 diabetes among patients with pre-diabetes at randomization |
| End point description:  |  |
| Time to CEC confirmed new onset of type 2 diabetes among those with pre-diabetes at randomization (i.e. excluding those that are normoglycemic at baseline) |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| From randomization up to approximately 6 years  |  |

| End point values            | Group I         | Group II        | Group III       | Group IV        |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1132            | 1094            | 1089            | 1645            |
| Units: Participants         | 169             | 171             | 161             | 246             |

## Statistical analyses

|   |                          |
|---|--------------------------|
| <b>Statistical analysis title</b>       | Analysis                 |
| Comparison groups                       | Group I v Group IV       |
| Number of subjects included in analysis | 2777                     |
| Analysis specification                  | Pre-specified            |
| Analysis type                           |                          |
| P-value                                 | = 0.8456 <sup>[29]</sup> |
| Method                                  | Logrank                  |
| Parameter estimate                      | Hazard ratio (HR)        |
| Point estimate                          | 1.01                     |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | 0.83                     |
| upper limit                             | 1.23                     |

Notes:

[29] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|   |                          |
|---|--------------------------|
| <b>Statistical analysis title</b>       | Analysis                 |
| Comparison groups                       | Group II v Group IV      |
| Number of subjects included in analysis | 2739                     |
| Analysis specification                  | Pre-specified            |
| Analysis type                           |                          |
| P-value                                 | = 0.8456 <sup>[30]</sup> |
| Method                                  | Logrank                  |
| Parameter estimate                      | Hazard ratio (HR)        |
| Point estimate                          | 1.06                     |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | 0.87                     |
| upper limit                             | 1.29                     |

Notes:

[30] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

|                                   |                      |
|-----------------------------------|----------------------|
| <b>Statistical analysis title</b> | Analysis             |
| Comparison groups                 | Group III v Group IV |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 2734                     |
| Analysis specification                  | Pre-specified            |
| Analysis type                           |                          |
| P-value                                 | = 0.6541 <sup>[31]</sup> |
| Method                                  | Logrank                  |
| Parameter estimate                      | Hazard ratio (HR)        |
| Point estimate                          | 0.98                     |
| Confidence interval                     |                          |
| level                                   | 95 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | 0.8                      |
| upper limit                             | 1.2                      |

Notes:

[31] - 1-sided adjusted for multiplicity using weighted Dunnett test. [significance level 0.0245]

### Secondary: Core phase all-cause mortality, non-fatal MI, or non-fatal stroke

|                 |   |
|-----------------|---|
| End point title | Core phase all-cause mortality, non-fatal MI, or non-fatal stroke |
|-----------------|---|

End point description:

Occurrence of the composite endpoint consisting of all-cause mortality, non-fatal IM, or non-fatal stroke

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomization, to end of treatment plus 30 days, up to approximately 6 years

| End point values            | Group I         | Group II        | Group III       | Group IV        |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2263            | 2284            | 2170            | 3344            |
| Units: Participants         | 403             | 395             | 394             | 661             |

### Statistical analyses

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>       | Analysis                |
| Comparison groups                       | Group I v Group IV      |
| Number of subjects included in analysis | 5607                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.028 <sup>[32]</sup> |
| Method                                  | Regression, Cox         |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.87                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.77                    |
| upper limit                             | 0.99                    |



Notes:

[32] - 2-sided unadjusted p-value

| Statistical analysis title              | Analysis                |
|---|-------------------------|
| Comparison groups                       | Group II v Group IV     |
| Number of subjects included in analysis | 5628                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.011 <sup>[33]</sup> |
| Method                                  | Regression, Cox         |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.85                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.75                    |
| upper limit                             | 0.96                    |

Notes:

[33] - 2-sided unadjusted p-value

| Statistical analysis title              | Analysis                |
|---|-------------------------|
| Comparison groups                       | Group III v Group IV    |
| Number of subjects included in analysis | 5514                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.377 <sup>[34]</sup> |
| Method                                  | Regression, Cox         |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.94                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.83                    |
| upper limit                             | 1.07                    |

Notes:

[34] - 2-sided unadjusted p-value

### Secondary: Core phase all-cause mortality

|   |                                |
|---|--------------------------------|
| End point title   | Core phase all-cause mortality |
| End point description:  |                                |
| Number of participant deaths  |                                |
| End point type  | Secondary                      |
| End point timeframe:  |                                |
| From randomization, to end of treatment plus 30 days, up to approximately 6 years |                                |

| End point values            | Group I         | Group II        | Group III       | Group IV        |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2263            | 2284            | 2170            | 3344            |
| Units: Participants         | 239             | 238             | 228             | 375             |

## Statistical analyses

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>       | Analysis                |
| Comparison groups                       | Group I v Group IV      |
| Number of subjects included in analysis | 5607                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.406 <sup>[35]</sup> |
| Method                                  | Regression, Cox         |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.93                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.79                    |
| upper limit                             | 1.1                     |

Notes:

[35] - 2-sided unadjusted p-value

|   |                         |
|---|-------------------------|
| <b>Statistical analysis title</b>       | Analysis                |
| Comparison groups                       | Group II v Group IV     |
| Number of subjects included in analysis | 5628                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.329 <sup>[36]</sup> |
| Method                                  | Regression, Cox         |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.92                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.78                    |
| upper limit                             | 1.09                    |

Notes:

[36] - 2-sided unadjusted p-value

|                                   |                      |
|-----------------------------------|----------------------|
| <b>Statistical analysis title</b> | Analysis             |
| Comparison groups                 | Group III v Group IV |

|   |                         |
|---|-------------------------|
| Number of subjects included in analysis | 5514                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           |                         |
| P-value                                 | = 0.597 <sup>[37]</sup> |
| Method                                  | Regression, Cox         |
| Parameter estimate                      | Hazard ratio (HR)       |
| Point estimate                          | 0.96                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.81                    |
| upper limit                             | 1.13                    |

Notes:

[37] - 2-sided unadjusted p-value

---

### Secondary: Substudy 1 (Core phase): Change from baseline of the total vessel wall area at month 3 in the bifurcation region of the Index Carotid Artery

---

|                 |  |
|-----------------|--|
| End point title | Substudy 1 (Core phase): Change from baseline of the total vessel wall area at month 3 in the bifurcation region of the Index Carotid Artery |
|-----------------|--|

End point description:

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| 3 months             |           |

| End point values            | Group I           | Group II          | Group III         | Group IV          |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 0 <sup>[38]</sup> | 0 <sup>[39]</sup> | 0 <sup>[40]</sup> | 0 <sup>[41]</sup> |
| Units: area                 |                   |                   |                   |                   |

Notes:

[38] - Analysis not performed

[39] - Analysis not performed

[40] - Analysis not performed

[41] - Analysis not performed

### Statistical analyses

---

No statistical analyses for this end point

---

### Secondary: Substudy 1 (Core phase): Mean total vessel wall area across the left and right carotid artery at Month 3 and Month 24

---

|                 |   |
|-----------------|---|
| End point title | Substudy 1 (Core phase): Mean total vessel wall area across the left and right carotid artery at Month 3 and Month 24 |
|-----------------|---|

End point description:

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| 24 months            |           |

| End point values            | Group I           | Group II          | Group III         | Group IV          |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 0 <sup>[42]</sup> | 0 <sup>[43]</sup> | 0 <sup>[44]</sup> | 0 <sup>[45]</sup> |
| Units: Mean area            |                   |                   |                   |                   |

Notes:

[42] - Analysis not performed

[43] - Analysis not performed

[44] - Analysis not performed

[45] - Analysis not performed

## Statistical analyses

No statistical analyses for this end point

### Secondary: Substudy 1 (Core phase): Change from baseline in corresponding total vessel wall area in the left and right carotid arteries

|                 |  |
|-----------------|--|
| End point title | Substudy 1 (Core phase): Change from baseline in corresponding total vessel wall area in the left and right carotid arteries |
|-----------------|--|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

24 months

| End point values            | Group I           | Group II          | Group III         | Group IV          |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 0 <sup>[46]</sup> | 0 <sup>[47]</sup> | 0 <sup>[48]</sup> | 0 <sup>[49]</sup> |
| Units: area                 |                   |                   |                   |                   |

Notes:

[46] - Analysis not performed

[47] - Analysis not performed

[48] - Analysis not performed

[49] - Analysis not performed

## Statistical analyses

No statistical analyses for this end point

### Secondary: Substudy 1 (Core phase): The existence of a baseline total vessel wall area by treatment interaction as well as the consistency of the treatment effect across subgroups

|                 |  |
|-----------------|--|
| End point title | Substudy 1 (Core phase): The existence of a baseline total vessel wall area by treatment interaction as well as the consistency of the treatment effect across subgroups |
|-----------------|--|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

24 months

| End point values            | Group I           | Group II          | Group III         | Group IV          |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 0 <sup>[50]</sup> | 0 <sup>[51]</sup> | 0 <sup>[52]</sup> | 0 <sup>[53]</sup> |
| Units: area                 |                   |                   |                   |                   |

Notes:

[50] - Analysis not performed

[51] - Analysis not performed

[52] - Analysis not performed

[53] - Analysis not performed

### Statistical analyses

No statistical analyses for this end point

### Secondary: Substudy 2: (Core phase) Change from baseline in insulin sensitivity index

|                 |  |
|-----------------|--|
| End point title | Substudy 2: (Core phase) Change from baseline in insulin sensitivity index |
|-----------------|--|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomization up to approximately 6 years

| End point values                 | Group I           | Group II          | Group III         | Group IV          |
|----------------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type               | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed      | 0 <sup>[54]</sup> | 0 <sup>[55]</sup> | 0 <sup>[56]</sup> | 0 <sup>[57]</sup> |
| Units: Insulin sensitivity index |                   |                   |                   |                   |

Notes:

[54] - Analysis not performed

[55] - Analysis not performed

[56] - Analysis not performed

[57] - Analysis not performed

### Statistical analyses

No statistical analyses for this end point

### Secondary: Substudy 2: (Core phase) Change from baseline in OGTT stimulated area under curve (AUC) 0-120 min of glucose concentration, insulin concentration, pro-insulin concentration, and Insulin Concentration/glucose Concentration Ratio

|  |   |
|--|---|
| End point title                                | Substudy 2: (Core phase) Change from baseline in OGTT stimulated area under curve (AUC) 0-120 min of glucose concentration, insulin concentration, pro-insulin concentration, and Insulin Concentration/glucose Concentration Ratio |
| End point description:                         |   |
| End point type                                 | Secondary   |
| End point timeframe:                           |   |
| From randomization up to approximately 6 years |   |

| End point values            | Group I           | Group II          | Group III         | Group IV          |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 0 <sup>[58]</sup> | 0 <sup>[59]</sup> | 0 <sup>[60]</sup> | 0 <sup>[61]</sup> |
| Units: AUC                  |                   |                   |                   |                   |

Notes:

[58] - Analysis not performed

[59] - Analysis not performed

[60] - Analysis not performed

[61] - Analysis not performed

### Statistical analyses

No statistical analyses for this end point

### Secondary: Substudy 2: (Core phase) Change from Baseline in Fasting Pro-Insulin Concentration/Insulin Concentration Ratio

|  |  |
|--|--|
| End point title                                | Substudy 2: (Core phase) Change from Baseline in Fasting Pro-Insulin Concentration/Insulin Concentration Ratio |
| End point description:                         |  |
| End point type                                 | Secondary  |
| End point timeframe:                           |  |
| From randomization up to approximately 6 years |  |

| End point values            | Group I           | Group II          | Group III         | Group IV          |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 0 <sup>[62]</sup> | 0 <sup>[63]</sup> | 0 <sup>[64]</sup> | 0 <sup>[65]</sup> |
| Units: Ratio                |                   |                   |                   |                   |

Notes:

[62] - Analysis not performed

[63] - Analysis not performed

[64] - Analysis not performed

[65] - Analysis not performed

### Statistical analyses

No statistical analyses for this end point

### Secondary: Substudy 2: (Core phase) Change from baseline in OGTT stimulated area under the curve (AUC) 0-120 min of C-peptide Concentration

|                 |  |
|-----------------|--|
| End point title | Substudy 2: (Core phase) Change from baseline in OGTT stimulated area under the curve (AUC) 0-120 min of C-peptide Concentration |
|-----------------|--|

End point description:

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomization up to approximately 6 years

| End point values            | Group I           | Group II          | Group III         | Group IV          |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 0 <sup>[66]</sup> | 0 <sup>[67]</sup> | 0 <sup>[68]</sup> | 0 <sup>[69]</sup> |
| Units: AUC                  |                   |                   |                   |                   |

Notes:

[66] - Analysis not performed

[67] - Analysis not performed

[68] - Analysis not performed

[69] - Analysis not performed

### Statistical analyses

No statistical analyses for this end point

### Secondary: Summary of Adverse Events (Core Phase)

|                 |  |
|-----------------|--|
| End point title | Summary of Adverse Events (Core Phase) |
|-----------------|--|

End point description:

Summary of Adverse Events (AEs) and Serious Adverse Events (SAEs) occurring during the double-blind Core phase of the study. AEs/SAEs are any signs or symptoms that occur during the study treatment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From randomization, to end of treatment plus 30 days, up to approximately 6 years

| End point values                          | Group I         | Group II             | Group III       | Group IV             |
|---|-----------------|----------------------|-----------------|----------------------|
| Subject group type                        | Reporting group | Reporting group      | Reporting group | Reporting group      |
| Number of subjects analysed               | 2263            | 2284 <sup>[70]</sup> | 2170            | 3344 <sup>[71]</sup> |
| Units: Participants                       |                 |                      |                 |                      |
| Patients with at least one AE             | 1987            | 1970                 | 1872            | 2915                 |
| AEs suspected to be related to study drug | 355             | 350                  | 267             | 474                  |
| Patients with at least one SAE            | 836             | 812                  | 741             | 1204                 |
| Discontinued due to SAEs                  | 135             | 130                  | 117             | 198                  |
| Discontinued due to non-serious AEs       | 40              | 34                   | 26              | 47                   |

|   |     |     |     |     |
|---|-----|-----|-----|-----|
| AEs leading to study treatment interruption | 268 | 270 | 228 | 399 |
|---|-----|-----|-----|-----|

Notes:

[70] - The number of subjects started was 2284; number of subjects analyzed was 2285

[71] - The number of subjects started was 3344; the number of subjects analyzed was 3348.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Summary of Adverse Events (Extension Phase)

|                 |   |
|-----------------|---|
| End point title | Summary of Adverse Events (Extension Phase) |
|-----------------|---|

End point description:

Summary of Adverse Events (AEs) and Serious Adverse Events (SAEs) occurring during the Extension phase of the study. AEs/SAEs are any signs or symptoms that occur during the study treatment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From start of Extension phase, to end of treatment plus 30 days, up to approximately 2 years

| End point values                            | Group I         | Group II        | Group III       | Group IV        |
|---|-----------------|-----------------|-----------------|-----------------|
| Subject group type                          | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed                 | 1267            | 1287            | 1279            | 1944            |
| Units: Participants                         |                 |                 |                 |                 |
| Patients with at least one AE               | 788             | 845             | 793             | 1250            |
| AEs suspected to be related to study drug   | 40              | 34              | 43              | 65              |
| Patients with at least one SAE              | 310             | 326             | 322             | 465             |
| Discontinued due to SAEs                    | 67              | 71              | 71              | 98              |
| Discontinued due to non-serious AEs         | 8               | 6               | 12              | 8               |
| AEs leading to study treatment interruption | 59              | 72              | 62              | 100             |

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Core Phase: From randomization, to end of treatment plus 30 days, up to approximately 6 years.

Extension Phase: From start of Extension phase, to end of treatment plus 30 days, up to approximately 2 years

Adverse event reporting additional description:

AEs/SAEs are any signs or symptoms that occur during the study treatment. During the Core phase, CV events being study endpoints were exempt from AE/SAE reporting; in contrast, during the Extension phase, all CV events were reported as AEs/SAEs. Groups I to IV show AE/SAEs during the Core phase; Group V shows AE/SAEs during the Extension phase.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 21.1   |

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Group I |
|-----------------------|---------|

Reporting group description:

Core phase: Blinded Canakinumab 300 mg quarterly subcutaneous + standard of care (SoC) therapy

Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|                       |          |
|-----------------------|----------|
| Reporting group title | Group II |
|-----------------------|----------|

Reporting group description:

Core phase: Blinded Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy.

Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|                       |           |
|-----------------------|-----------|
| Reporting group title | Group III |
|-----------------------|-----------|

Reporting group description:

Core phase: Blinded Canakinumab 50 mg quarterly subcutaneous + standard of care (SoC) therapy

Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|                       |          |
|-----------------------|----------|
| Reporting group title | Group IV |
|-----------------------|----------|

Reporting group description:

Core phase: Blinded matching placebo quarterly subcutaneous + standard of care (SoC) therapy

Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

|                       |         |
|-----------------------|---------|
| Reporting group title | Group V |
|-----------------------|---------|

Reporting group description:

Extension phase: Switched to open-label Canakinumab 150 mg quarterly subcutaneous + standard of care (SoC) therapy

| Serious adverse events                            | Group I                | Group II               | Group III              |
|---|------------------------|------------------------|------------------------|
| Total subjects affected by serious adverse events |                        |                        |                        |
| subjects affected / exposed                       | 759 / 2263<br>(33.54%) | 743 / 2285<br>(32.52%) | 686 / 2170<br>(31.61%) |
| number of deaths (all causes)                     | 239                    | 240                    | 228                    |
| number of deaths resulting from adverse events    | 9                      | 9                      | 11                     |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |                  |
| Abdominal neoplasm  |                  |                  |                  |
| subjects affected / exposed   | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0            |
| Acute leukaemia   |                  |                  |                  |
| subjects affected / exposed   | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 1            | 0 / 0            |
| Acute myeloid leukaemia   |                  |                  |                  |
| subjects affected / exposed   | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0            |
| Adenocarcinoma  |                  |                  |                  |
| subjects affected / exposed   | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 1            | 0 / 1            |
| Adenocarcinoma gastric  |                  |                  |                  |
| subjects affected / exposed   | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 1 / 2            | 0 / 2            |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 1            | 0 / 0            |
| Adenocarcinoma of colon   |                  |                  |                  |
| subjects affected / exposed   | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all                     | 1 / 3            | 0 / 1            | 2 / 2            |
| deaths causally related to treatment / all                          | 0 / 1            | 0 / 0            | 2 / 2            |
| Adenocarcinoma pancreas   |                  |                  |                  |
| subjects affected / exposed   | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0            |
| Adenoma benign  |                  |                  |                  |
| subjects affected / exposed   | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            | 0 / 0            |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| Adenosquamous cell lung cancer<br>subjects affected / exposed | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to<br>treatment / all            | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 0             |
| Adrenal adenoma<br>subjects affected / exposed                | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to<br>treatment / all            | 0 / 1             | 0 / 0             | 0 / 1             |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 0             |
| Adrenal neoplasm<br>subjects affected / exposed               | 1 / 2263 (0.04%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to<br>treatment / all            | 0 / 1             | 0 / 1             | 0 / 0             |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 0             |
| Angiolipoma<br>subjects affected / exposed                    | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to<br>treatment / all            | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 0             |
| Angiosarcoma<br>subjects affected / exposed                   | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to<br>treatment / all            | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 0             |
| B-cell lymphoma<br>subjects affected / exposed                | 2 / 2263 (0.09%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to<br>treatment / all            | 0 / 2             | 0 / 0             | 0 / 0             |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 0             |
| Basal cell carcinoma<br>subjects affected / exposed           | 14 / 2263 (0.62%) | 18 / 2285 (0.79%) | 18 / 2170 (0.83%) |
| occurrences causally related to<br>treatment / all            | 3 / 15            | 0 / 22            | 0 / 19            |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 0             |
| Benign cardiac neoplasm<br>subjects affected / exposed        | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to<br>treatment / all            | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to<br>treatment / all                 | 0 / 0             | 0 / 0             | 0 / 1             |
| Benign gastric neoplasm                                       |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign lung neoplasm                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign neoplasm                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign neoplasm of bladder                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign neoplasm of scrotum                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign neoplasm of skin                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign salivary gland neoplasm                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign small intestinal neoplasm                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign urinary tract neoplasm                   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bile duct cancer                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bladder cancer                                  |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 5 / 2285 (0.22%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 1 / 6            | 1 / 5            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |
| Bladder neoplasm                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bladder papilloma                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bladder transitional cell carcinoma             |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 2            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Bone cancer                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bone cancer metastatic                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bowen's disease                                 |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Brain neoplasm                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Brain neoplasm malignant                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Breast cancer                                   |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 0 / 2285 (0.00%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 0            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Breast cancer female                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Breast cancer metastatic                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 1            | 0 / 0            |
| Brenner tumour                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchial carcinoma                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Carcinoid tumour of the gastrointestinal tract  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cervix carcinoma                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cholangiocarcinoma                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 2            | 0 / 0            |
| Chronic lymphocytic leukaemia                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Clear cell renal cell carcinoma                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Colon adenoma                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Colon cancer                                    |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 4 / 2285 (0.18%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 2 / 3            | 0 / 4            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 1            |
| Colon neoplasm                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Colorectal adenocarcinoma                       |                  |                  |                  |

|  |                  |                  |                  |
|--|------------------|------------------|------------------|
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Colorectal cancer                                    |                  |                  |                  |
| subjects affected / exposed                          | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Diffuse large B-cell lymphoma                        |                  |                  |                  |
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Diffuse large B-cell lymphoma stage IV               |                  |                  |                  |
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Ductal adenocarcinoma of pancreas                    |                  |                  |                  |
| subjects affected / exposed                          | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Endometrial adenocarcinoma                           |                  |                  |                  |
| subjects affected / exposed                          | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Endometrial cancer                                   |                  |                  |                  |
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Endometrial cancer stage III                         |                  |                  |                  |
| subjects affected / exposed                          | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| Extranodal marginal zone B-cell lymphoma (MALT type) |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fibroma   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fibrous histiocytoma                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gallbladder adenocarcinoma                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastric adenoma                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastric cancer                                  |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 5            | 1 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 0            | 0 / 1            |
| Gastrointestinal carcinoma                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Gastrointestinal tract adenoma                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Glioblastoma                                    |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Glioma  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemangioma                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic cancer                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 1            |
| Hepatic cancer metastatic                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |
| Hepatic cancer stage IV                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic neoplasm                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatocellular carcinoma                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Hodgkin's disease                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypergammaglobulinaemia benign monoclonal       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Inflammatory pseudotumour                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intestinal adenocarcinoma                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intraductal proliferative breast lesion         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Invasive breast carcinoma                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Invasive ductal breast carcinoma                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Keratoacanthoma                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Large intestine benign neoplasm                 |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Laryngeal cancer                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Laryngeal squamous cell carcinoma               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lentigo maligna                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Leukaemia                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lip and/or oral cavity cancer                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 1            | 0 / 0            |
| Lip squamous cell carcinoma                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lipoma  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Liposarcoma                                     |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung adenocarcinoma                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 3 / 2285 (0.13%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 3            | 0 / 2            |
| Lung adenocarcinoma stage III                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung adenocarcinoma stage IV                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Lung cancer metastatic                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            | 0 / 0            |
| Lung carcinoma cell type unspecified recurrent  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung carcinoma cell type unspecified stage III  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung neoplasm                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung neoplasm malignant                         |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 9 / 2285 (0.39%) | 9 / 2170 (0.41%) |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 10           | 1 / 10           |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 4            | 1 / 8            |
| Lung squamous cell carcinoma metastatic         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lymphoma  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Lymphoproliferative disorder                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Malignant fibrous histiocytoma                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malignant mediastinal neoplasm                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malignant melanoma                              |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 5 / 2285 (0.22%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5            | 1 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malignant melanoma in situ                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malignant neoplasm of pleura                    |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malignant neoplasm of unknown primary site      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malignant peritoneal neoplasm                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 1 / 1            |
| Malignant pleural effusion                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Mantle cell lymphoma                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Medullary thyroid cancer                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meningioma                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meningioma benign                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metastases to adrenals                          |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Metastases to bone                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Metastases to central nervous system            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Metastases to kidney                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Metastases to liver                             |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 5 / 2285 (0.22%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 5            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 3            | 0 / 1            |
| Metastases to lung                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            | 0 / 4            |
| Metastases to lymph nodes                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 2            |
| Metastases to pelvis                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metastases to pleura                            |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Metastases to rectum                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metastases to spine                             |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 1            |
| Metastatic bronchial carcinoma                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metastatic malignant melanoma                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metastatic renal cell carcinoma                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            | 0 / 0            |
| Metastatic squamous cell carcinoma              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Monoclonal gammopathy                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mucinous adenocarcinoma of appendix             |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Mycosis fungoides</b>                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Myelodysplastic syndrome</b>                 |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| <b>Myelofibrosis</b>                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Nasal cavity cancer</b>                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Neoplasm malignant</b>                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Neoplasm skin</b>                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Neuroendocrine breast tumour</b>             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Neuroendocrine carcinoma</b>                 |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Non-Hodgkin's lymphoma                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Non-Hodgkin's lymphoma refractory               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 1 / 1            |
| Non-small cell lung cancer                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Non-small cell lung cancer metastatic           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Non-small cell lung cancer stage IV             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 1 / 1            |
| Oesophageal adenocarcinoma                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Oesophageal adenocarcinoma stage II             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal cancer metastatic                   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0            | 0 / 0            |
| Oesophageal carcinoma                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 1 / 4            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 1            |
| Oesophageal neoplasm                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal squamous cell carcinoma             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oligodendroglioma                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oropharyngeal squamous cell carcinoma           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ovarian adenoma                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ovarian cancer                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ovarian neoplasm                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancreatic carcinoma                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 4 / 2285 (0.18%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 4            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 4            | 0 / 3            |
| Pancreatic carcinoma metastatic                 |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 1 / 2            | 0 / 1            | 0 / 0            |
| Papillary cystadenoma lymphomatosum             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Papillary renal cell carcinoma                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Papillary thyroid cancer                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Parathyroid tumour benign                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Penile cancer                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Phaeochromocytoma                               |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pharyngeal cancer                               |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0             |
| Pituitary tumour benign                         |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Plasma cell myeloma                             |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pleomorphic adenoma                             |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Polycythaemia vera                              |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Prostate cancer                                 |                   |                   |                   |
| subjects affected / exposed                     | 12 / 2263 (0.53%) | 10 / 2285 (0.44%) | 10 / 2170 (0.46%) |
| occurrences causally related to treatment / all | 2 / 12            | 0 / 10            | 1 / 10            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Prostate cancer metastatic                      |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0             |
| Prostate cancer recurrent                       |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prostatic adenoma                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectal adenocarcinoma                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectal adenoma                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectal cancer                                   |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 2            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            | 0 / 0            |
| Rectal cancer metastatic                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectosigmoid cancer                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal cancer                                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 2            | 0 / 2            |
| Renal cancer metastatic                         |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal cell carcinoma                            |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 1 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 1 / 3            |
| Renal neoplasm                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal oncocytoma                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rosai-Dorfman syndrome                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Salivary gland adenoma                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Salivary gland neoplasm                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Seborrhoeic keratosis                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Skin cancer                                     |                  |                  |                  |



|   |                   |                  |                  |
|---|-------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Small cell lung cancer                          |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 1            |
| Small cell lung cancer metastatic               |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Small intestine adenocarcinoma                  |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Small intestine carcinoma                       |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Small intestine carcinoma metastatic            |                   |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Squamous cell carcinoma                         |                   |                  |                  |
| subjects affected / exposed                     | 12 / 2263 (0.53%) | 5 / 2285 (0.22%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 2 / 12            | 0 / 6            | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 1            |
| Squamous cell carcinoma of lung                 |                   |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 5 / 2285 (0.22%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 5            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 3            | 0 / 0            |
| Squamous cell carcinoma of skin                 |                   |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Squamous cell carcinoma of the hypopharynx      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Squamous cell carcinoma of the tongue           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Superficial spreading melanoma stage II         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Testis cancer                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Throat cancer                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Thyroid cancer                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thyroid cancer metastatic                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thyroid neoplasm                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tongue neoplasm malignant stage unspecified     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 1            |
| Tonsil cancer metastatic                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Transitional cell carcinoma                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Transitional cell carcinoma urethra             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tumour perforation                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Uterine cancer                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Uterine leiomyoma                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular disorders                              |                  |                  |                  |
| Accelerated hypertension                        |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Aneurysm ruptured                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Angiodysplasia                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Aortic aneurysm                                 |                  |                  |                  |
| subjects affected / exposed                     | 8 / 2263 (0.35%) | 4 / 2285 (0.18%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 4            | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Aortic aneurysm rupture                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Aortic dissection                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Aortic stenosis                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Aortitis  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Arterial haemorrhage                            |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arterial insufficiency                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arteriosclerosis                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arteriovenous fistula                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arteritis                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Brachiocephalic artery stenosis                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Circulatory collapse                            |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Deep vein thrombosis                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Embolism  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Embolism arterial                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Embolism venous                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Essential hypertension                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Extremity necrosis                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Femoral artery aneurysm                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Femoral artery embolism                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haematoma                                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 3 / 2285 (0.13%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemodynamic instability                        |                  |                  |                  |

|   |                   |                  |                  |
|---|-------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Haemorrhage                                     |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Hypertension                                    |                   |                  |                  |
| subjects affected / exposed                     | 10 / 2263 (0.44%) | 8 / 2285 (0.35%) | 8 / 2170 (0.37%) |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 8            | 0 / 8            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Hypertensive crisis                             |                   |                  |                  |
| subjects affected / exposed                     | 7 / 2263 (0.31%)  | 5 / 2285 (0.22%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 6            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Hypertensive emergency                          |                   |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Hypotension                                     |                   |                  |                  |
| subjects affected / exposed                     | 8 / 2263 (0.35%)  | 5 / 2285 (0.22%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 5            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Hypovolaemic shock                              |                   |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            | 0 / 0            |
| Intermittent claudication                       |                   |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Internal haemorrhage                            |                   |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ischaemic limb pain                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lymphatic fistula                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lymphorrhoea                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malignant hypertension                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Orthostatic hypertension                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Orthostatic hypotension                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 3 / 2285 (0.13%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 3            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pallor  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral arterial occlusive disease           |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 4 / 2285 (0.18%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Peripheral artery aneurysm                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral artery occlusion                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 3 / 2285 (0.13%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral artery stenosis                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral artery thrombosis                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Peripheral embolism                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral ischaemia                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral vascular disorder                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 3 / 2285 (0.13%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Peripheral venous disease                       |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Shock   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Shock haemorrhagic                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Temporal arteritis                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thrombophlebitis                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Thrombophlebitis superficial                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thrombosis                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Varicose ulceration                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Varicose vein                                   |                  |                  |                  |

|  |                  |                   |                  |
|--|------------------|-------------------|------------------|
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 1 / 2285 (0.04%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1             | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0             | 0 / 0            |
| Vascular insufficiency                               |                  |                   |                  |
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0             | 0 / 0            |
| Venous thrombosis limb                               |                  |                   |                  |
| subjects affected / exposed                          | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0             | 0 / 0            |
| General disorders and administration site conditions |                  |                   |                  |
| Adverse drug reaction                                |                  |                   |                  |
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0             | 0 / 0            |
| Asthenia   |                  |                   |                  |
| subjects affected / exposed                          | 4 / 2263 (0.18%) | 2 / 2285 (0.09%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all      | 0 / 4            | 0 / 2             | 0 / 1            |
| deaths causally related to treatment / all           | 0 / 1            | 0 / 0             | 0 / 0            |
| Cardiac death  |                  |                   |                  |
| subjects affected / exposed                          | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0             | 0 / 0            |
| Chest discomfort                                     |                  |                   |                  |
| subjects affected / exposed                          | 2 / 2263 (0.09%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 2            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0             | 0 / 0            |
| Chest pain   |                  |                   |                  |
| subjects affected / exposed                          | 3 / 2263 (0.13%) | 12 / 2285 (0.53%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all      | 0 / 3            | 1 / 14            | 0 / 2            |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0             | 0 / 0            |
| Chills   |                  |                   |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Complication associated with device             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Death   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 1 / 1            |
| Drowning  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Drug intolerance                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Exercise tolerance decreased                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Facial pain                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fatigue   |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gait disturbance                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| General physical health deterioration           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Generalised oedema                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hernia  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Heteroplasia                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperplasia                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypothermia                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Impaired healing                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Implant site irritation                         |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Incarcerated hernia                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Inflammation                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Influenza like illness                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Injection site reaction                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ischaemic ulcer                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Local swelling                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Malaise   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mass  |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Multiple organ dysfunction syndrome             |                   |                   |                   |
| subjects affected / exposed                     | 3 / 2263 (0.13%)  | 2 / 2285 (0.09%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 1             | 0 / 0             |
| Necrosis  |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Non-cardiac chest pain                          |                   |                   |                   |
| subjects affected / exposed                     | 44 / 2263 (1.94%) | 48 / 2285 (2.10%) | 39 / 2170 (1.80%) |
| occurrences causally related to treatment / all | 0 / 57            | 0 / 53            | 0 / 41            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Oedema peripheral                               |                   |                   |                   |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pacemaker syndrome                              |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pain  |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Polyp   |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pseudocyst                                      |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pyrexia   |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 4 / 2285 (0.18%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Stent-graft endoleak                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sudden cardiac death                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 1            |
| Sudden death                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Surgical failure                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Systemic inflammatory response syndrome         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 2 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular stent restenosis                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular stent stenosis                         |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular stent thrombosis                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vessel puncture site haemorrhage                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Immune system disorders                         |                  |                  |                  |
| Allergy to arthropod sting                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anaphylactic reaction                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anaphylactic shock                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Contrast media allergy                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Drug hypersensitivity                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypersensitivity                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Social circumstances                            |                  |                  |                  |
| Homicide  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Reproductive system and breast disorders        |                  |                  |                  |
| Balanoposthitis                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Benign prostatic hyperplasia                    |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 6 / 2285 (0.26%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cystocele                                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dysmenorrhoea                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Endometrial hyperplasia                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Epididymal cyst                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| Erectile dysfunction                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Female genital tract fistula                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Genital atrophy                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Genital prolapse                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Menorrhagia                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ovarian cyst                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pelvic pain                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Postmenopausal haemorrhage                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prostatic haemorrhage                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prostatic mass                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prostatism                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prostatitis                                     |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prostatomegaly                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectocele                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spermatocele                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Uterine cervix stenosis                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Uterine prolapse                                |                  |                  |                  |

|   |                   |                  |                   |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0             |
| Vaginal haemorrhage                             |                   |                  |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0             |
| Varicocele                                      |                   |                  |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0             |
| Varicose veins pelvic                           |                   |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0             |
| Respiratory, thoracic and mediastinal disorders |                   |                  |                   |
| Acute pulmonary oedema                          |                   |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 3 / 2285 (0.13%) | 4 / 2170 (0.18%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 3            | 0 / 4             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 1             |
| Acute respiratory distress syndrome             |                   |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0             |
| Acute respiratory failure                       |                   |                  |                   |
| subjects affected / exposed                     | 10 / 2263 (0.44%) | 7 / 2285 (0.31%) | 11 / 2170 (0.51%) |
| occurrences causally related to treatment / all | 1 / 11            | 0 / 7            | 1 / 12            |
| deaths causally related to treatment / all      | 1 / 4             | 0 / 2            | 0 / 0             |
| Alveolitis                                      |                   |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0             |
| Alveolitis allergic                             |                   |                  |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Asphyxia  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Asthma  |                  |                  |                  |
| subjects affected / exposed                     | 7 / 2263 (0.31%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 2 / 8            | 1 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atelectasis                                     |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchial hyperreactivity                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchial obstruction                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchiectasis                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchitis chronic                              |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bronchospasm                                    |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Cheyne-Stokes respiration                       |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Chronic obstructive pulmonary disease           |                   |                   |                   |
| subjects affected / exposed                     | 28 / 2263 (1.24%) | 21 / 2285 (0.92%) | 16 / 2170 (0.74%) |
| occurrences causally related to treatment / all | 2 / 48            | 2 / 23            | 1 / 21            |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 2             | 0 / 2             |
| Cough   |                   |                   |                   |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Dyspnoea  |                   |                   |                   |
| subjects affected / exposed                     | 14 / 2263 (0.62%) | 8 / 2285 (0.35%)  | 10 / 2170 (0.46%) |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 9             | 0 / 10            |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             | 0 / 0             |
| Dyspnoea exertional                             |                   |                   |                   |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 1 / 2285 (0.04%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Dyspnoea paroxysmal nocturnal                   |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Emphysema                                       |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Epistaxis                                       |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemoptysis                                     |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Haemothorax                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hiccups   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hydrothorax                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypopnoea                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoxia   |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Idiopathic interstitial pneumonia               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Idiopathic pneumonia syndrome                   |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Idiopathic pulmonary fibrosis                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Interstitial lung disease                       |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 2 / 2            |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 0            | 0 / 0            |
| Laryngeal oedema                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Laryngospasm                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung consolidation                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung hernia                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung infiltration                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Nasal obstruction                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nasal polyps                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nasal turbinate hypertrophy                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Obstructive airways disorder                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Organising pneumonia                            |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0            | 0 / 0            |
| Oropharyngeal pain                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pickwickian syndrome                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pleural adhesion                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pleural effusion                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 8 / 2263 (0.35%) | 5 / 2285 (0.22%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 10           | 1 / 5            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Pleurisy  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 3 / 2285 (0.13%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pleuritic pain                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumomediastinum                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumonia aspiration                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 4 / 2285 (0.18%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |
| Pneumonitis                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Pneumothorax                                    |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumothorax spontaneous                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Productive cough                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulmonary alveolar haemorrhage                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulmonary arterial hypertension                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulmonary congestion                            |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulmonary embolism                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Pulmonary fibrosis                              |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Pulmonary haematoma                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulmonary hypertension                          |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 3 / 2285 (0.13%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulmonary mass                                  |                  |                  |                  |

|   |                   |                   |                  |
|---|-------------------|-------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 2 / 2285 (0.09%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Pulmonary microemboli                           |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Pulmonary oedema                                |                   |                   |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%)  | 4 / 2285 (0.18%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 4             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0            |
| Pulmonary sarcoidosis                           |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Respiratory alkalosis                           |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Respiratory arrest                              |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 1            |
| Respiratory distress                            |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 2 / 2285 (0.09%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Respiratory failure                             |                   |                   |                  |
| subjects affected / exposed                     | 12 / 2263 (0.53%) | 11 / 2285 (0.48%) | 9 / 2170 (0.41%) |
| occurrences causally related to treatment / all | 0 / 14            | 1 / 11            | 0 / 9            |
| deaths causally related to treatment / all      | 0 / 5             | 0 / 6             | 0 / 3            |
| Respiratory tract inflammation                  |                   |                   |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Respiratory tract irritation                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rhinitis allergic                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinus congestion                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinus polyp                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sleep apnoea syndrome                           |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Status asthmaticus                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vocal cord leukoplakia                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wheezing  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Psychiatric disorders                               |                  |                  |                  |
| Acute stress disorder                               |                  |                  |                  |
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Adjustment disorder                                 |                  |                  |                  |
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Affective disorder                                  |                  |                  |                  |
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Alcoholic psychosis                                 |                  |                  |                  |
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Alcoholism  |                  |                  |                  |
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Anxiety   |                  |                  |                  |
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Anxiety disorder                                    |                  |                  |                  |
| subjects affected / exposed                         | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            | 0 / 0            |
| Anxiety disorder due to a general medical condition |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Bipolar I disorder                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bipolar disorder                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Burnout syndrome                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Completed suicide                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Confusional state                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Conversion disorder                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Delirium  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Delirium tremens                                |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Depression                                      |                  |                  |                  |
| subjects affected / exposed                     | 7 / 2263 (0.31%) | 4 / 2285 (0.18%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Dissociative amnesia                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Drug use disorder                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Generalised anxiety disorder                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hallucination, visual                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Head banging                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Homicidal ideation                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Insomnia  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                           | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Intentional self-injury                               |                  |                  |                  |
| subjects affected / exposed                           | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Major depression                                      |                  |                  |                  |
| subjects affected / exposed                           | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all       | 0 / 2            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Mental status changes                                 |                  |                  |                  |
| subjects affected / exposed                           | 4 / 2263 (0.18%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all       | 0 / 8            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Panic attack  |                  |                  |                  |
| subjects affected / exposed                           | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Personality change                                    |                  |                  |                  |
| subjects affected / exposed                           | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Psychotic disorder                                    |                  |                  |                  |
| subjects affected / exposed                           | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Psychotic disorder due to a general medical condition |                  |                  |                  |
| subjects affected / exposed                           | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            | 0 / 0            |
| Restlessness  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Schizophrenia                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Somnambulism                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Suicidal ideation                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Suicide attempt                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Product issues                                  |                  |                  |                  |
| Device battery issue                            |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device dislocation                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device end of service                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device failure                                  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device inappropriate shock delivery             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device issue                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device lead damage                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device lead issue                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device loosening                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device malfunction                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device occlusion                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device signal detection issue                   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lead dislodgement                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatobiliary disorders                         |                  |                  |                  |
| Acute hepatic failure                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Alcoholic liver disease                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Autoimmune hepatitis                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bile duct stenosis                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bile duct stone                                 |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Biliary cirrhosis                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Biliary colic                                   |                  |                  |                  |

|   |                   |                  |                  |
|---|-------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Biliary dilatation                              |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Biliary fistula                                 |                   |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Cholangitis                                     |                   |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 2 / 2285 (0.09%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2            | 1 / 4            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Cholangitis acute                               |                   |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            | 0 / 0            |
| Cholecystitis                                   |                   |                  |                  |
| subjects affected / exposed                     | 11 / 2263 (0.49%) | 4 / 2285 (0.18%) | 8 / 2170 (0.37%) |
| occurrences causally related to treatment / all | 1 / 11            | 0 / 4            | 0 / 8            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 1            |
| Cholecystitis acute                             |                   |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%)  | 7 / 2285 (0.31%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 5             | 1 / 7            | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Cholelithiasis                                  |                   |                  |                  |
| subjects affected / exposed                     | 8 / 2263 (0.35%)  | 8 / 2285 (0.35%) | 8 / 2170 (0.37%) |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 9            | 0 / 9            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Cholestasis                                     |                   |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Drug-induced liver injury                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gallbladder polyp                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhagic hepatic cyst                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic cirrhosis                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic congestion                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic failure                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Hepatic function abnormal                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic steatosis                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic vein thrombosis                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Hepatitis                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatitis toxic                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatomegaly                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatorenal failure                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatosplenomegaly                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Hydrocholecystis                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ischaemic hepatitis                             |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Jaundice cholestatic                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Liver disorder                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Liver injury                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Non-alcoholic fatty liver                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Non-alcoholic steatohepatitis                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Portal vein thrombosis                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Steatohepatitis                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Investigations                                  |                  |                  |                  |
| Alanine aminotransferase increased              |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anticoagulation drug level above therapeutic    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Aspartate aminotransferase increased            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood creatine phosphokinase MB increased       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood creatine phosphokinase increased          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood creatinine increased                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood glucose increased                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood magnesium decreased                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| Blood pressure increased                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood urine present                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Body mass index decreased                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Central venous pressure increased               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chest X-ray abnormal                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Clostridium test positive                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ejection fraction decreased                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemoglobin decreased                           |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic enzyme increased                        |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| Human metapneumovirus test positive                       |                  |                  |                  |
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| Imaging procedure abnormal                                |                  |                  |                  |
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| International normalised ratio decreased                  |                  |                  |                  |
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| International normalised ratio increased                  |                  |                  |                  |
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| Liver function test abnormal                              |                  |                  |                  |
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| Liver function test increased                             |                  |                  |                  |
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| N-terminal prohormone brain natriuretic peptide increased |                  |                  |                  |
| subjects affected / exposed                               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| Oxygen saturation decreased<br>subjects affected / exposed        | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to<br>treatment / all                | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Platelet count decreased<br>subjects affected / exposed           | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to<br>treatment / all                | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Quality of life decreased<br>subjects affected / exposed          | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to<br>treatment / all                | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Scan myocardial perfusion abnormal<br>subjects affected / exposed | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to<br>treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Troponin T increased<br>subjects affected / exposed               | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to<br>treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Troponin increased<br>subjects affected / exposed                 | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to<br>treatment / all                | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Volume blood decreased<br>subjects affected / exposed             | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to<br>treatment / all                | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Weight decreased<br>subjects affected / exposed                   | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to<br>treatment / all                | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to<br>treatment / all                     | 0 / 0            | 0 / 0            | 0 / 0            |
| Weight increased  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| White blood cell count increased                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Injury, poisoning and procedural complications  |                  |                  |                  |
| Abdominal injury                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Accident  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Accidental overdose                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Acetabulum fracture                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Alcohol poisoning                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anaemia postoperative                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anastomotic leak                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Animal bite                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ankle fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 0            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arterial injury                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arthropod sting                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Asbestosis                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bone contusion                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Brain contusion                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiac function disturbance postoperative      |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Central cord syndrome                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cervical vertebral fracture                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chest injury                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Clavicle fracture                               |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Closed globe injury                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Comminuted fracture                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Concussion                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Contusion                                       |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Coronary artery restenosis                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Craniocerebral injury                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dural tear                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Epicondylitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Face injury                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Facial bones fracture                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fall  |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Femoral neck fracture                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 5 / 2285 (0.22%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Femur fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 3 / 2285 (0.13%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Foot fracture                                   |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Forearm fracture                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Foreign body                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fracture displacement                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gallbladder injury                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrointestinal stoma complication             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrointestinal stoma necrosis                 |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Gun shot wound                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hand fracture                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Head injury                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hip fracture                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Humerus fracture                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Incision site haemorrhage                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Incision site pain                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Incisional hernia                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Incisional hernia, obstructive                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Injury  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intentional overdose                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intentional product misuse                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Jaw fracture                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Joint dislocation                               |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Joint injury                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Laceration                                      |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ligament injury                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Ligament rupture                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ligament sprain                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Limb injury                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Limb traumatic amputation                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lower limb fracture                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lumbar vertebral fracture                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meniscus injury                                 |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 3 / 2285 (0.13%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Multiple fractures                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Multiple injuries                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscle contusion                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Muscle rupture                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscle strain                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Musculoskeletal foreign body                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nerve injury                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Overdose  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Patella fracture                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pelvic fracture                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral artery restenosis                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Periprosthetic fracture                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Perirenal haematoma                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumoconiosis                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumothorax traumatic                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural complication                    |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural discharge                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural fever                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural haematoma                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural haemorrhage                     |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Postoperative hernia                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Postoperative wound complication                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Procedural complication                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Procedural intestinal perforation               |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Procedural pain                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pubis fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Radiation mucositis                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Radius fracture                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rib fracture                                    |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 3 / 2285 (0.13%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Road traffic accident                           |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            | 0 / 0            |
| Scapula fracture                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Scratch   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Seroma  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Skeletal injury                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Skin laceration                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Skull fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal column injury                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal compression fracture                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal cord injury                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal cord injury cervical                     |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal fracture                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Splenic rupture                                 |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Stab wound                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sternal fracture                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Stress fracture                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Subarachnoid haemorrhage                        |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Subdural haematoma                              |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 4 / 2285 (0.18%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Subdural haemorrhage                            |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tendon injury                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tendon rupture                                  |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thermal burn                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thoracic vertebral fracture                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tibia fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tooth fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Toxicity to various agents                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Tracheal haemorrhage                            |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Traumatic amputation                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Traumatic arthritis                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Traumatic haematoma                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Traumatic haemothorax                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Traumatic intracranial haemorrhage              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ulna fracture                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Upper limb fracture                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Urinary retention postoperative                 |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular graft complication                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular pseudoaneurysm                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular pseudoaneurysm ruptured                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wound dehiscence                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wound secretion                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wrist fracture                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Congenital, familial and genetic disorders      |                  |                  |                  |
| Atrial septal defect                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Branchial cyst                                  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebrovascular arteriovenous malformation      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhagic arteriovenous malformation         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hereditary haemochromatosis                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hydrocele                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nonketotic hyperglycinaemia                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Phimosis  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pyloric stenosis                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tracheo-oesophageal fistula                     |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             | 0 / 0             |
| Cardiac disorders                               |                   |                   |                   |
| Acute coronary syndrome                         |                   |                   |                   |
| subjects affected / exposed                     | 6 / 2263 (0.27%)  | 1 / 2285 (0.04%)  | 4 / 2170 (0.18%)  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 1             | 0 / 4             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 2             |
| Acute left ventricular failure                  |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Acute myocardial infarction                     |                   |                   |                   |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 2 / 2285 (0.09%)  | 2 / 2170 (0.09%)  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             | 0 / 2             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0             |
| Adams-Stokes syndrome                           |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Angina pectoris                                 |                   |                   |                   |
| subjects affected / exposed                     | 42 / 2263 (1.86%) | 41 / 2285 (1.79%) | 37 / 2170 (1.71%) |
| occurrences causally related to treatment / all | 0 / 51            | 0 / 52            | 0 / 43            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Angina unstable                                 |                   |                   |                   |
| subjects affected / exposed                     | 39 / 2263 (1.72%) | 34 / 2285 (1.49%) | 37 / 2170 (1.71%) |
| occurrences causally related to treatment / all | 0 / 50            | 0 / 45            | 0 / 37            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Aortic valve incompetence                       |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0             |
| Aortic valve stenosis                           |                   |                   |                   |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arrhythmia                                      |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Arrhythmia supraventricular                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arteriosclerosis coronary artery                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arteriospasm coronary                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atrial fibrillation                             |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 6 / 2285 (0.26%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Atrial flutter                                  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atrial tachycardia                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atrial thrombosis                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atrioventricular block                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atrioventricular block complete                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atrioventricular block first degree             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Atrioventricular block second degree            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 4 / 2285 (0.18%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bradyarrhythmia                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bradycardia                                     |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 4            | 1 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiac aneurysm                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiac arrest                                  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 7 / 2285 (0.31%) | 7 / 2170 (0.32%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 7            | 0 / 7            |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 5            | 0 / 4            |
| Cardiac discomfort                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiac failure                                 |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 4 / 2285 (0.18%) | 7 / 2170 (0.32%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 4            | 0 / 8            |
| deaths causally related to treatment / all      | 0 / 4            | 0 / 1            | 0 / 0            |
| Cardiac failure acute                           |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 1            | 0 / 0            |
| Cardiac failure chronic                         |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Cardiac failure congestive                      |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |
| Cardiac fibrillation                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiac pseudoaneurysm                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiac tamponade                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiac ventricular thrombosis                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardio-respiratory arrest                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 3            |
| Cardiogenic shock                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 3 / 2285 (0.13%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 3            |
| Cardiomegaly                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiomyopathy                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cardiopulmonary failure                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Conduction disorder                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Congestive cardiomyopathy                       |                  |                  |                  |

|   |                  |                   |                  |
|---|------------------|-------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Cor pulmonale                                   |                  |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Coronary artery disease                         |                  |                   |                  |
| subjects affected / exposed                     | 9 / 2263 (0.40%) | 10 / 2285 (0.44%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 1 / 10           | 0 / 13            | 0 / 8            |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1             | 0 / 0            |
| Coronary artery insufficiency                   |                  |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Coronary artery occlusion                       |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Coronary artery stenosis                        |                  |                   |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Hypertensive heart disease                      |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             | 0 / 0            |
| Intracardiac thrombus                           |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Ischaemic cardiomyopathy                        |                  |                   |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 5 / 2285 (0.22%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Left ventricular dysfunction                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Left ventricular failure                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Left ventricular hypertrophy                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Microvascular coronary artery disease           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mitral valve incompetence                       |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 3 / 2285 (0.13%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5            | 1 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Myocardial infarction                           |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            | 0 / 5            |
| Myocardial ischaemia                            |                  |                  |                  |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 3 / 2285 (0.13%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 3            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 2            | 0 / 0            |
| Nodal arrhythmia                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Palpitations                                    |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pericardial effusion                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pericarditis                                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prinzmetal angina                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulseless electrical activity                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Right ventricular dysfunction                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Right ventricular failure                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Silent myocardial infarction                    |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinus arrest                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinus bradycardia                               |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinus node dysfunction                          |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinus tachycardia                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Stress cardiomyopathy                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Supraventricular tachycardia                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tachyarrhythmia                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tachycardia                                     |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Torsade de pointes                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tricuspid valve incompetence                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Trifascicular block                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ventricular arrhythmia                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ventricular extrasystoles                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ventricular fibrillation                        |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 9 / 2285 (0.39%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 9            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Ventricular tachyarrhythmia                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ventricular tachycardia                         |                  |                  |                  |

|   |                   |                  |                  |
|---|-------------------|------------------|------------------|
| subjects affected / exposed                     | 10 / 2263 (0.44%) | 5 / 2285 (0.22%) | 9 / 2170 (0.41%) |
| occurrences causally related to treatment / all | 0 / 13            | 0 / 6            | 0 / 9            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Nervous system disorders                        |                   |                  |                  |
| Amnesia   |                   |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Amyotrophic lateral sclerosis                   |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            | 0 / 0            |
| Aphasia   |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Apraxia   |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Ataxia  |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Balance disorder                                |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Brain injury                                    |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 3 / 2285 (0.13%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            | 0 / 0            |
| Brain oedema                                    |                   |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Carotid arteriosclerosis                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Carotid artery aneurysm                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Carotid artery disease                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Carotid artery occlusion                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Carotid artery stenosis                         |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Carpal tunnel syndrome                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cauda equina syndrome                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebellar infarction                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebellar stroke                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebral arteriosclerosis                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebral haemorrhage                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebral infarction                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebral ischaemia                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cerebrovascular accident                        |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Cervical myelopathy                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cervical radiculopathy                          |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cervicobrachial syndrome                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cognitive disorder                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Coma  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Dementia  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dementia Alzheimer's type                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dementia with Lewy bodies                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Depressed level of consciousness                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diabetic coma                                   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diabetic neuropathy                             |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diplegia  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dizziness                                       |                  |                  |                  |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dysaesthesia                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dysarthria                                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dystonia  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Embolic stroke                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Encephalopathy                                  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Epilepsy  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Facial paralysis                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Focal dyscognitive seizures                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Generalised tonic-clonic seizure                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Guillain-Barre syndrome                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhage intracranial                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Haemorrhagic stroke                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhagic transformation stroke              |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Headache  |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 3 / 2285 (0.13%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hemiparesis                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hydrocephalus                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypersomnia                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypertensive encephalopathy                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoaesthesia                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoglycaemic coma                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoglycaemic encephalopathy                    |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoxic-ischaemic encephalopathy                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| IIIrd nerve paresis                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intracranial aneurysm                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intracranial pressure increased                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ischaemic stroke                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lacunar infarction                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lacunar stroke                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Loss of consciousness                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 3 / 2285 (0.13%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lumbar radiculopathy                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lumbosacral radiculopathy                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mental impairment                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metabolic encephalopathy                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Migraine  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mixed dementia                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nerve compression                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Neuralgia                                       |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Neuropathy peripheral                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Normal pressure hydrocephalus                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Optic neuritis                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Orthostatic intolerance                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Paraesthesia                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Paralysis                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Paresis   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Partial seizures                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peripheral nerve lesion                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Polyneuropathy                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post herpetic neuralgia                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post stroke seizure                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Presyncope                                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Restless legs syndrome                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sciatica  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Seizure   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sensory disturbance                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal claudication                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal cord compression                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal cord infarction                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spondylitic myelopathy                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Status epilepticus                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Stupor  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Subdural hygroma                                |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Syncope   |                   |                   |                   |
| subjects affected / exposed                     | 15 / 2263 (0.66%) | 17 / 2285 (0.74%) | 16 / 2170 (0.74%) |
| occurrences causally related to treatment / all | 0 / 16            | 1 / 19            | 2 / 17            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Tension headache                                |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Thalamic infarction                             |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Thrombotic cerebral infarction                  |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Tonic convulsion                                |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             | 0 / 0             |
| Toxic encephalopathy                            |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Transient global amnesia                        |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Transient ischaemic attack                      |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Trigeminal neuralgia                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Upper motor neurone lesion                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| VIth nerve paralysis                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vascular dementia                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Vascular encephalopathy                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vertebrobasilar insufficiency                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blood and lymphatic system disorders            |                  |                  |                  |
| Abnormal clotting factor                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anaemia   |                  |                  |                  |

|   |                   |                   |                  |
|---|-------------------|-------------------|------------------|
| subjects affected / exposed                     | 15 / 2263 (0.66%) | 10 / 2285 (0.44%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 1 / 15            | 0 / 11            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 2             | 0 / 0            |
| Bone marrow oedema                              |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Coagulopathy                                    |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Disseminated intravascular coagulation          |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Febrile neutropenia                             |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Haemorrhagic anaemia                            |                   |                   |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%)  | 2 / 2285 (0.09%)  | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 2             | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Heparin-induced thrombocytopenia                |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0            |
| Hilar lymphadenopathy                           |                   |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0            |
| Histiocytosis haematophagic                     |                   |                   |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypochromic anaemia                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Immune thrombocytopenic purpura                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Iron deficiency anaemia                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Leukocytosis                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Leukopenia                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lymphadenitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lymphadenopathy                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lymphadenopathy mediastinal                     |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Microcytic anaemia                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Monoclonal B-cell lymphocytosis                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Normochromic normocytic anaemia                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Normocytic anaemia                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancytopenia                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 1 / 1            | 0 / 0            |
| Polycythaemia                                   |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Splenic infarction                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Splenomegaly                                    |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thrombocytopenia                                |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 0            | 1 / 3            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Thrombocytopenic purpura                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ear and labyrinth disorders                     |                  |                  |                  |
| Cerumen impaction                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ear pain  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoacusis                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meniere's disease                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Otosclerosis                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Presbycusis                                     |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sudden hearing loss                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tympanic membrane perforation                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vertigo   |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 5 / 2285 (0.22%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vertigo positional                              |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Eye disorders                                   |                  |                  |                  |
| Amaurosis fugax                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Angle closure glaucoma                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blindness                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blindness transient                             |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blindness unilateral                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cataract  |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 8 / 2285 (0.35%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 10           | 0 / 8            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cataract cortical                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cataract diabetic                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cataract nuclear                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Corneal degeneration                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Corneal infiltrates                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dacryostenosis acquired                         |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diabetic retinopathy                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Eye haemorrhage                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Eyelid ptosis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Glaucoma  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Iridocyclitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lens dislocation                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Macular degeneration                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Macular fibrosis                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Macular hole                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Macular oedema                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Neovascular age-related macular degeneration    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ocular ischaemic syndrome                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Papilloedema                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Retinal artery thrombosis                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Retinal detachment                              |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Retinal haemorrhage                             |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Retinal vein occlusion                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Retinal vein thrombosis                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vitreous haemorrhage                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrointestinal disorders                      |                  |                  |                  |
| Abdominal adhesions                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abdominal discomfort                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abdominal distension                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abdominal hernia                                |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abdominal pain                                  |                  |                  |                  |



|   |                  |                  |                   |
|---|------------------|------------------|-------------------|
| subjects affected / exposed                     | 7 / 2263 (0.31%) | 4 / 2285 (0.18%) | 10 / 2170 (0.46%) |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 4            | 1 / 10            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Abdominal pain lower                            |                  |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 2             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Abdominal pain upper                            |                  |                  |                   |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%)  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 2            | 0 / 3             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Acute abdomen                                   |                  |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Alcoholic pancreatitis                          |                  |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Anal fissure                                    |                  |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Anal haemorrhage                                |                  |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Anal skin tags                                  |                  |                  |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0             |
| Anal ulcer                                      |                  |                  |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anal ulcer haemorrhage                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anorectal disorder                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Appendiceal mucocoele                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Appendix disorder                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ascites   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Change of bowel habit                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chronic gastritis                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Colitis   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 3 / 2285 (0.13%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Colitis ischaemic                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |
| Colitis microscopic                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Colitis ulcerative                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Colonic fistula                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Constipation                                    |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Crohn's disease                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 3 / 2285 (0.13%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dental caries                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diabetic gastroenteropathy                      |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diarrhoea                                       |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 5 / 2285 (0.22%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            | 1 / 5            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Dieulafoy's vascular malformation               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diverticulum                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diverticulum intestinal                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diverticulum intestinal haemorrhagic            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Duodenal stenosis                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Duodenal ulcer                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Duodenal ulcer haemorrhage                      |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Duodenal ulcer perforation                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Duodenitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dyspepsia                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dysphagia                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Enteritis                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Enterocolitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Enterovesical fistula                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Epigastric discomfort                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Erosive duodenitis                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Erosive oesophagitis                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Faecaloma                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Faeces discoloured                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Flatulence                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Food poisoning                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gallstone ileus                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastric haemorrhage                             |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastric ulcer                                   |                  |                  |                  |
| subjects affected / exposed                     | 7 / 2263 (0.31%) | 6 / 2285 (0.26%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 6            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastric ulcer haemorrhage                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastric ulcer perforation                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastric volvulus                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastritis                                       |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 1 / 2285 (0.04%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastritis erosive                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastritis haemorrhagic                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastroduodenitis                                |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Gastrointestinal angiodysplasia                 |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Gastrointestinal disorder                       |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Gastrointestinal erosion                        |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Gastrointestinal haemorrhage                    |                   |                   |                   |
| subjects affected / exposed                     | 13 / 2263 (0.57%) | 16 / 2285 (0.70%) | 14 / 2170 (0.65%) |
| occurrences causally related to treatment / all | 0 / 13            | 1 / 23            | 0 / 18            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             | 0 / 3             |
| Gastrointestinal necrosis                       |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Gastrointestinal pain                           |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Gastrointestinal perforation                    |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Gastrointestinal ulcer                          |                   |                   |                   |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrointestinal vascular malformation          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrooesophageal reflux disease                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 5 / 2285 (0.22%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haematemesis                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haematochezia                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 3 / 2285 (0.13%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhagic necrotic pancreatitis              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhoidal haemorrhage                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhoids                                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 3 / 2285 (0.13%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhoids thrombosed                         |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hiatus hernia                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ileal ulcer                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ileus   |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Ileus paralytic                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Impaired gastric emptying                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Incarcerated inguinal hernia                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Incarcerated umbilical hernia                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Inflammatory bowel disease                      |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Inguinal hernia                                 |                  |                  |                  |
| subjects affected / exposed                     | 8 / 2263 (0.35%) | 5 / 2285 (0.22%) | 7 / 2170 (0.32%) |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 5            | 0 / 8            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Inguinal hernia strangulated                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intestinal fistula                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intestinal haemorrhage                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intestinal infarction                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intestinal ischaemia                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intestinal mass                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intestinal obstruction                          |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Intestinal perforation                          |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Intestinal ulcer                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Irritable bowel syndrome                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ischaemic enteritis                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Large intestinal obstruction                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Large intestinal stenosis                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Large intestine perforation                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Large intestine polyp                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 4 / 2285 (0.18%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lower gastrointestinal haemorrhage              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 4 / 2285 (0.18%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Mallory-Weiss syndrome                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Melaena   |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mesenteric artery stenosis                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mesenteric artery thrombosis                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |
| Mesenteric vascular insufficiency               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Mouth cyst                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mouth ulceration                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Narcotic bowel syndrome                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nausea  |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 3 / 2285 (0.13%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Obstruction gastric                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Odynophagia                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal obstruction                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal perforation                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal rupture                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal stenosis                            |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal ulcer                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal varices haemorrhage                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophagitis                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancreatic cyst                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Pancreatic disorder                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancreatic duct dilatation                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancreatic mass                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancreatic pseudocyst                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancreatitis                                    |                  |                  |                  |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 6 / 2285 (0.26%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 6            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Pancreatitis acute                              |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 6 / 2285 (0.26%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 1            |
| Pancreatitis chronic                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pancreatitis necrotising                        |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peptic ulcer                                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peptic ulcer haemorrhage                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peritoneal haemorrhage                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumatosis intestinalis                        |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumoperitoneum                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Proctalgia                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Proctitis                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ranula  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectal haemorrhage                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 6 / 2285 (0.26%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectal lesion                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectal perforation                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rectal polyp                                    |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Retroperitoneal haematoma                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Retroperitoneal haemorrhage                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Salivary gland calculus                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Small intestinal haemorrhage                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Small intestinal obstruction                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Small intestinal perforation                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Small intestine ulcer                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Subileus  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Thrombosis mesenteric vessel                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Umbilical hernia                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 4 / 2285 (0.18%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Upper gastrointestinal haemorrhage              |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 8 / 2285 (0.35%) | 8 / 2170 (0.37%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 8            | 2 / 8            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vomiting  |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 4 / 2285 (0.18%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 4            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |
| Skin and subcutaneous tissue disorders          |                  |                  |                  |
| Acne  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Actinic keratosis                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Angioedema                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Blister   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Brow ptosis                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Decubitus ulcer                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dermatitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Dermatitis allergic                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diabetic foot                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 6 / 2285 (0.26%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Eczema  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Erythema  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperhidrosis                                   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperkeratosis                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypersensitivity vasculitis                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Neurodermatitis                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prurigo   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pruritus allergic                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Psoriasis                                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rhinophyma                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Skin ulcer                                      |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 5 / 2285 (0.22%)  | 5 / 2170 (0.23%)  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 6             | 0 / 6             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Stasis dermatitis                               |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Stevens-Johnson syndrome                        |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Subcutaneous emphysema                          |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Urticaria                                       |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Renal and urinary disorders                     |                   |                   |                   |
| Acute kidney injury                             |                   |                   |                   |
| subjects affected / exposed                     | 20 / 2263 (0.88%) | 30 / 2285 (1.31%) | 16 / 2170 (0.74%) |
| occurrences causally related to treatment / all | 1 / 21            | 0 / 31            | 0 / 20            |
| deaths causally related to treatment / all      | 0 / 4             | 0 / 3             | 0 / 2             |
| Acute prerenal failure                          |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Anuria  |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Azotaemia                                       |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Calculus bladder                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Calculus urethral                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Calculus urinary                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chronic kidney disease                          |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 5 / 2285 (0.22%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 5            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 1            |
| Diabetic nephropathy                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dysuria   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| End stage renal disease                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Focal segmental glomerulosclerosis              |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Glomerulonephritis membranous                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haematuria                                      |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 6 / 2285 (0.26%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 6            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Hydronephrosis                                  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 3 / 2285 (0.13%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypertensive nephropathy                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lower urinary tract symptoms                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nephrolithiasis                                 |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Nephrotic syndrome                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Obstructive uropathy                            |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pollakiuria                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Polyuria  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Prerenal failure                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal artery stenosis                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal artery thrombosis                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Renal colic                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal cyst                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal failure                                   |                  |                  |                  |

|   |                  |                   |                   |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed                     | 7 / 2263 (0.31%) | 10 / 2285 (0.44%) | 11 / 2170 (0.51%) |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 11            | 0 / 11            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 4             | 0 / 2             |
| Renal haematoma                                 |                  |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0             |
| Renal impairment                                |                  |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 4 / 2285 (0.18%)  | 3 / 2170 (0.14%)  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4             | 0 / 3             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0             |
| Renal injury                                    |                  |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0             |
| Renal mass                                      |                  |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 1             |
| Renal tubular necrosis                          |                  |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0             |
| Stress urinary incontinence                     |                  |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0             |
| Tubulointerstitial nephritis                    |                  |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0             |
| Ureteric obstruction                            |                  |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ureteric stenosis                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ureterolithiasis                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Urethral obstruction                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Urinary bladder haemorrhage                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Urinary bladder polyp                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Urinary incontinence                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Urinary retention                               |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 4 / 2285 (0.18%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Urinary tract obstruction                       |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vesicocutaneous fistula                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Endocrine disorders                             |                  |                  |                  |
| Goitre  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperparathyroidism primary                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperthyroidism                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypopituitarism                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypothyroidism                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Inappropriate antidiuretic hormone secretion    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Primary hyperaldosteronism                      |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Toxic goitre                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Musculoskeletal and connective tissue disorders |                  |                  |                  |
| Arthralgia                                      |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 5 / 2285 (0.22%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arthritis                                       |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arthritis reactive                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arthropathy                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Back pain                                       |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 8 / 2285 (0.35%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 8            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bone pain                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Bursitis  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cervical spinal stenosis                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chondromalacia                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chondropathy                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Compartment syndrome                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Costochondritis                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dactylitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dupuytren's contracture                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Exostosis                                       |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fasciitis                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Finger deformity                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Flank pain                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Foot deformity                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fracture malunion                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gouty arthritis                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gouty tophus                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Groin pain                                      |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemarthrosis                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Immunoglobulin G4 related disease               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Intervertebral disc calcification               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intervertebral disc compression                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intervertebral disc degeneration                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intervertebral disc disorder                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intervertebral disc displacement                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Intervertebral disc protrusion                  |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 2 / 2285 (0.09%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Jaw cyst  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Joint instability                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Joint swelling                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lumbar spinal stenosis                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 4 / 2285 (0.18%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meniscal degeneration                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metatarsalgia                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscle atrophy                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscle haemorrhage                              |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscle spasms                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscle swelling                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscular weakness                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Musculoskeletal chest pain                      |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 3 / 2285 (0.13%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            | 0 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Musculoskeletal pain                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Myalgia   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Myofascial pain syndrome                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Neck pain                                       |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Neuropathic arthropathy                         |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Osteitis  |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Osteoarthritis                                  |                   |                   |                   |
| subjects affected / exposed                     | 19 / 2263 (0.84%) | 21 / 2285 (0.92%) | 18 / 2170 (0.83%) |
| occurrences causally related to treatment / all | 0 / 22            | 0 / 24            | 0 / 20            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Osteochondrosis                                 |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 2 / 2285 (0.09%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Osteolysis                                      |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Osteonecrosis                                   |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Osteoporosis                                    |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Osteoporotic fracture                           |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pain in extremity                               |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pain in jaw                                     |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pathological fracture                           |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Polyarthritis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Polymyalgia rheumatica                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rhabdomyolysis                                  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rheumatoid arthritis                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Rotator cuff syndrome                           |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Shoulder deformity                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Soft tissue mass                                |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Spinal column stenosis                          |                  |                  |                  |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 2 / 2285 (0.09%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal deformity                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal osteoarthritis                           |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spinal pain                                     |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spondylitis                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Spondylolisthesis                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Synovial cyst                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Synovitis                                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tendonitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tenosynovitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Trigger finger                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vertebral foraminal stenosis                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vertebral wedging                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Infections and infestations                     |                  |                  |                  |
| Abdominal abscess                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abdominal infection                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abdominal sepsis                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abscess intestinal                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abscess jaw                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abscess limb                                    |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 4            | 1 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abscess neck                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abscess oral                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Abscess soft tissue                             |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Acute hepatitis B                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Acute sinusitis                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Anal abscess                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Appendicitis                                    |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 4 / 2285 (0.18%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 4            | 1 / 6            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Appendicitis perforated                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arthritis bacterial                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Arthritis infective                             |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Atypical pneumonia                              |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Bacteraemia</b>                              |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 2            | 1 / 1            | 0 / 0            |
| <b>Bacterial disease carrier</b>                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Bacterial pyelonephritis</b>                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Bacterial sepsis</b>                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| <b>Bacteroides infection</b>                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Bartholin's abscess</b>                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Beta haemolytic streptococcal infection</b>  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Bone abscess</b>                             |                  |                  |                  |

|   |                   |                  |                  |
|---|-------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Bronchitis                                      |                   |                  |                  |
| subjects affected / exposed                     | 10 / 2263 (0.44%) | 9 / 2285 (0.39%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 11            | 1 / 9            | 1 / 8            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            | 0 / 0            |
| Bronchitis bacterial                            |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Bursitis infective                              |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Bursitis infective staphylococcal               |                   |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Campylobacter gastroenteritis                   |                   |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Campylobacter infection                         |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Candida infection                               |                   |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            | 0 / 0            |
| Carbuncle                                       |                   |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Cellulitis                                      |                   |                   |                   |
| subjects affected / exposed                     | 29 / 2263 (1.28%) | 32 / 2285 (1.40%) | 19 / 2170 (0.88%) |
| occurrences causally related to treatment / all | 6 / 35            | 9 / 37            | 2 / 21            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0             |
| Cellulitis gangrenous                           |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Cellulitis of male external genital organ       |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Cellulitis staphylococcal                       |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Central nervous system infection                |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Chikungunya virus infection                     |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Cholangitis infective                           |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 2             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Cholecystitis infective                         |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chorioretinitis                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chronic sinusitis                               |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Chronic tonsillitis                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Clostridial infection                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Clostridium difficile colitis                   |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 1            | 1 / 5            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Clostridium difficile infection                 |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 1            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Colonic abscess                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Conjunctivitis                                  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Corona virus infection                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Creutzfeldt-Jakob disease                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Cystitis  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Dengue fever                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device related infection                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Device related sepsis                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diabetic foot infection                         |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Diabetic gangrene                               |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diarrhoea infectious                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Diverticulitis                                  |                  |                  |                  |
| subjects affected / exposed                     | 8 / 2263 (0.35%) | 9 / 2285 (0.39%) | 8 / 2170 (0.37%) |
| occurrences causally related to treatment / all | 0 / 9            | 1 / 9            | 4 / 8            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Ear infection                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Empyema   |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Endocarditis                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Endocarditis bacterial                          |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Enteritis infectious                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Epididymitis                                    |                  |                  |                  |

|   |                  |                   |                  |
|---|------------------|-------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Epiglottitis                                    |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Erysipelas                                      |                  |                   |                  |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 12 / 2285 (0.53%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 1 / 8            | 2 / 13            | 1 / 6            |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0             | 0 / 0            |
| Escherichia sepsis                              |                  |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%)  | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Escherichia urinary tract infection             |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| External ear cellulitis                         |                  |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Folliculitis                                    |                  |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Fungal skin infection                           |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Furuncle  |                  |                   |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gallbladder abscess                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gallbladder empyema                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gangrene  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 5 / 2170 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 7            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Gastritis viral                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastroenteritis                                 |                  |                  |                  |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 5 / 2285 (0.22%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 5            | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Gastroenteritis clostridial                     |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 2 / 3            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastroenteritis rotavirus                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastroenteritis salmonella                      |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastroenteritis viral                           |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrointestinal bacterial infection            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrointestinal infection                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gastrointestinal viral infection                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Groin infection                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haematoma infection                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemophilus infection                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemophilus sepsis                              |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Haemorrhagic pneumonia                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 1 / 1            |
| Helicobacter infection                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hepatic amoebiasis                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Hepatitis viral                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Herpes ophthalmic                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Herpes zoster                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Human ehrlichiosis                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypopyon  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Implant site abscess                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Implant site infection                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Incision site cellulitis                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Incision site infection                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Infected bite                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Infected cyst                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Infected skin ulcer                             |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Infection                                       |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                                   | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Infectious colitis  |                  |                  |                  |
| subjects affected / exposed                                   | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Infectious pleural effusion                                   |                  |                  |                  |
| subjects affected / exposed                                   | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 3            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Infective exacerbation of chronic obstructive airways disease |                  |                  |                  |
| subjects affected / exposed                                   | 5 / 2263 (0.22%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all               | 1 / 9            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Infective spondylitis   |                  |                  |                  |
| subjects affected / exposed                                   | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Influenza   |                  |                  |                  |
| subjects affected / exposed                                   | 4 / 2263 (0.18%) | 6 / 2285 (0.26%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all               | 0 / 4            | 0 / 6            | 0 / 2            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Intervertebral discitis                                       |                  |                  |                  |
| subjects affected / exposed                                   | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Joint abscess   |                  |                  |                  |
| subjects affected / exposed                                   | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            | 0 / 0            |
| Labyrinthitis   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Leptospirosis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Liver abscess                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Localised infection                             |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 1 / 3            | 1 / 2            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lower respiratory tract infection               |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 1 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung abscess                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lung infection                                  |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Lyme disease                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lymphangitis                                    |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malaria   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mastoiditis                                     |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mediastinitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Medical device site infection                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meningitis                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meningitis bacterial                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Meningococcal sepsis                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mesenteric abscess                              |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metapneumovirus infection                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Muscle abscess                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mycobacterial infection                         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Mycobacterium avium complex infection           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Necrotising fasciitis                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Neutropenic sepsis                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Oesophageal candidiasis                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Orchitis  |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Osteomyelitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 3 / 2285 (0.13%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 4            | 1 / 3            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Osteomyelitis bacterial                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Osteomyelitis blastomyces                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Otitis externa                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Otitis media                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Otitis media acute                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Otitis media chronic                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Pancreatic abscess                              |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Parainfluenzae virus infection                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Parametritis                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Paronychia                                      |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Parotitis                                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pelvic abscess                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Perichondritis                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Perineal abscess                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Periodontitis                                   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Periorbital cellulitis                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Perirectal abscess                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peritoneal abscess                              |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Peritonitis                                     |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 2 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pharyngeal abscess                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pharyngitis                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pharyngitis streptococcal                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pilonidal cyst                                  |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pneumococcal sepsis                             |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pneumonia                                       |                   |                   |                   |
| subjects affected / exposed                     | 67 / 2263 (2.96%) | 60 / 2285 (2.63%) | 53 / 2170 (2.44%) |
| occurrences causally related to treatment / all | 13 / 72           | 15 / 69           | 9 / 58            |
| deaths causally related to treatment / all      | 1 / 13            | 2 / 12            | 2 / 9             |
| Pneumonia bacterial                             |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pneumonia escherichia                           |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pneumonia haemophilus                           |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pneumonia klebsiella                            |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pneumonia legionella                            |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Pneumonia necrotising                           |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumonia pneumococcal                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumonia pseudomonal                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pneumonia staphylococcal                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural cellulitis                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural infection                       |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Post procedural sepsis                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Postoperative abscess                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Postoperative wound infection                   |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Proctitis infectious                            |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Propionibacterium infection                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pseudomembranous colitis                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 1            |
| Pseudomonal bacteraemia                         |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pseudomonas bronchitis                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pseudomonas infection                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 1 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Psoas abscess                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pulmonary sepsis                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Pulmonary tuberculosis                          |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pyelitis  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pyelonephritis                                  |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 2            | 1 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pyelonephritis acute                            |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 5 / 2285 (0.22%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Pyoderma  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Pyuria  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Renal abscess                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Respiratory tract infection                     |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%)  | 7 / 2285 (0.31%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 2             | 2 / 7             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             | 0 / 0             |
| Respiratory tract infection viral               |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Rhinitis  |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Rubella   |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Salmonellosis                                   |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Scrotal abscess                                 |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 1 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Scrub typhus                                    |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Sepsis  |                   |                   |                   |
| subjects affected / exposed                     | 19 / 2263 (0.84%) | 25 / 2285 (1.09%) | 15 / 2170 (0.69%) |
| occurrences causally related to treatment / all | 5 / 19            | 9 / 25            | 3 / 15            |
| deaths causally related to treatment / all      | 3 / 7             | 2 / 12            | 0 / 6             |
| Sepsis syndrome                                 |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Septic embolus                                  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Septic necrosis                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Septic shock                                    |                  |                  |                  |
| subjects affected / exposed                     | 6 / 2263 (0.27%) | 8 / 2285 (0.35%) | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 8            | 2 / 6            |
| deaths causally related to treatment / all      | 0 / 5            | 0 / 6            | 1 / 5            |
| Sialoadenitis                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinusitis                                       |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Sinusitis fungal                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Staphylococcal abscess                          |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Staphylococcal bacteraemia                      |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 2            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Staphylococcal infection                        |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Staphylococcal mediastinitis                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Staphylococcal sepsis                           |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Streptococcal bacteraemia                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Streptococcal sepsis                            |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Subcutaneous abscess                            |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 3 / 2285 (0.13%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 2 / 4            | 0 / 3            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Subdiaphragmatic abscess                        |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Subdural empyema                                |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Testicular abscess                              |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tetanus   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tonsillitis                                     |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tooth abscess                                   |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tracheobronchitis                               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Tuberculosis                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Upper respiratory tract infection               |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Urinary tract infection                         |                  |                  |                  |

|   |                   |                   |                   |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed                     | 13 / 2263 (0.57%) | 11 / 2285 (0.48%) | 10 / 2170 (0.46%) |
| occurrences causally related to treatment / all | 3 / 13            | 5 / 12            | 0 / 10            |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 0             | 0 / 0             |
| Urinary tract infection bacterial               |                   |                   |                   |
| subjects affected / exposed                     | 3 / 2263 (0.13%)  | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%)  |
| occurrences causally related to treatment / all | 1 / 3             | 0 / 0             | 0 / 1             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Urinary tract infection enterococcal            |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Urinary tract infection fungal                  |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Urinary tract infection pseudomonal             |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Urosepsis                                       |                   |                   |                   |
| subjects affected / exposed                     | 4 / 2263 (0.18%)  | 4 / 2285 (0.18%)  | 5 / 2170 (0.23%)  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 4             | 1 / 5             |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             | 0 / 0             |
| Vestibular neuronitis                           |                   |                   |                   |
| subjects affected / exposed                     | 1 / 2263 (0.04%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Viral cardiomyopathy                            |                   |                   |                   |
| subjects affected / exposed                     | 0 / 2263 (0.00%)  | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             | 0 / 0             |
| Viral diarrhoea                                 |                   |                   |                   |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Viral infection                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Viral upper respiratory tract infection         |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Vulval abscess                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wound infection                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 3 / 2285 (0.13%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            | 1 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wound infection bacterial                       |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wound infection staphylococcal                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Wound sepsis                                    |                  |                  |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Metabolism and nutrition disorders              |                  |                  |                  |
| Acidosis  |                  |                  |                  |

|   |                  |                   |                  |
|---|------------------|-------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             | 0 / 0            |
| Cachexia  |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             | 0 / 0            |
| Dehydration                                     |                  |                   |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 6 / 2285 (0.26%)  | 6 / 2170 (0.28%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 7             | 0 / 6            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             | 0 / 2            |
| Diabetes mellitus                               |                  |                   |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 10 / 2285 (0.44%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 10            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             | 0 / 0            |
| Diabetes mellitus inadequate control            |                  |                   |                  |
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 1 / 2285 (0.04%)  | 7 / 2170 (0.32%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1             | 0 / 8            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Diabetes with hyperosmolarity                   |                  |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             | 0 / 0            |
| Diabetic complication                           |                  |                   |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%)  | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             | 0 / 0            |
| Diabetic ketoacidosis                           |                  |                   |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%)  | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             | 0 / 0            |
| Diabetic metabolic decompensation               |                  |                   |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Electrolyte imbalance                           |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Fluid overload                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Gout  |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperammonaemia                                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypercalcaemia                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperchloraemia                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperglycaemia                                  |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 4 / 2285 (0.18%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperglycaemic hyperosmolar nonketotic syndrome |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperkalaemia                                   |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 4 / 2285 (0.18%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Hypermagnesaemia                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyperuricaemia                                  |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoalbuminaemia                                |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            | 0 / 0            |
| Hypocalcaemia                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypoglycaemia                                   |                  |                  |                  |
| subjects affected / exposed                     | 4 / 2263 (0.18%) | 4 / 2285 (0.18%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 1 / 4            | 1 / 4            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypokalaemia                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 3 / 2170 (0.14%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 3            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypomagnesaemia                                 |                  |                  |                  |

|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 2 / 2263 (0.09%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hyponatraemia                                   |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 2 / 2285 (0.09%) | 4 / 2170 (0.18%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            | 0 / 4            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Hypovolaemia                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Insulin resistant diabetes                      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Insulin-requiring type 2 diabetes mellitus      |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Ketoacidosis                                    |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 0 / 2285 (0.00%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Lactic acidosis                                 |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 0 / 2285 (0.00%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| Malnutrition                                    |                  |                  |                  |
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            | 0 / 0            |
| Metabolic acidosis                              |                  |                  |                  |



|   |                  |                  |                  |
|---|------------------|------------------|------------------|
| subjects affected / exposed                     | 1 / 2263 (0.04%) | 2 / 2285 (0.09%) | 2 / 2170 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            | 0 / 2            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 2            | 0 / 1            |
| <b>Obesity</b>                                  |                  |                  |                  |
| subjects affected / exposed                     | 5 / 2263 (0.22%) | 1 / 2285 (0.04%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Type 1 diabetes mellitus</b>                 |                  |                  |                  |
| subjects affected / exposed                     | 0 / 2263 (0.00%) | 1 / 2285 (0.04%) | 0 / 2170 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0            |
| <b>Type 2 diabetes mellitus</b>                 |                  |                  |                  |
| subjects affected / exposed                     | 3 / 2263 (0.13%) | 2 / 2285 (0.09%) | 1 / 2170 (0.05%) |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            | 0 / 0            |

| <b>Serious adverse events</b>  | Group IV             | Group V              |  |
|--|----------------------|----------------------|--|
| <b>Total subjects affected by serious adverse events</b>                   |                      |                      |  |
| subjects affected / exposed  | 1099 / 3348 (32.83%) | 1216 / 5777 (21.05%) |  |
| number of deaths (all causes)  | 378                  | 211                  |  |
| number of deaths resulting from adverse events                             | 8                    | 7                    |  |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |                      |                      |  |
| <b>Abdominal neoplasm</b>  |                      |                      |  |
| subjects affected / exposed  | 1 / 3348 (0.03%)     | 1 / 5777 (0.02%)     |  |
| occurrences causally related to treatment / all                            | 0 / 1                | 0 / 1                |  |
| deaths causally related to treatment / all                                 | 0 / 1                | 0 / 0                |  |
| <b>Acute leukaemia</b>   |                      |                      |  |
| subjects affected / exposed  | 0 / 3348 (0.00%)     | 0 / 5777 (0.00%)     |  |
| occurrences causally related to treatment / all                            | 0 / 0                | 0 / 0                |  |
| deaths causally related to treatment / all                                 | 0 / 0                | 0 / 0                |  |
| <b>Acute myeloid leukaemia</b>   |                      |                      |  |
| subjects affected / exposed  | 0 / 3348 (0.00%)     | 1 / 5777 (0.02%)     |  |
| occurrences causally related to treatment / all                            | 0 / 0                | 0 / 1                |  |
| deaths causally related to treatment / all                                 | 0 / 0                | 0 / 0                |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Adenocarcinoma                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0            |  |
| Adenocarcinoma gastric                          |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Adenocarcinoma of colon                         |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Adenocarcinoma pancreas                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Adenoma benign                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adenosquamous cell lung cancer                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adrenal adenoma                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adrenal neoplasm                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Angiolipoma                                     |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Angiosarcoma                                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| B-cell lymphoma                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Basal cell carcinoma                            |                   |                   |  |
| subjects affected / exposed                     | 21 / 3348 (0.63%) | 30 / 5777 (0.52%) |  |
| occurrences causally related to treatment / all | 0 / 32            | 3 / 33            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign cardiac neoplasm                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign gastric neoplasm                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign lung neoplasm                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign neoplasm                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign neoplasm of bladder                      |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign neoplasm of scrotum                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign neoplasm of skin                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign salivary gland neoplasm                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign small intestinal neoplasm                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign urinary tract neoplasm                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bile duct cancer                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Bladder cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 3 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Bladder neoplasm                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder papilloma                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder transitional cell carcinoma             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone cancer                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Bone cancer metastatic                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bowen's disease                                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain neoplasm malignant                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast cancer                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast cancer female                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brenner tumour                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchial carcinoma                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 2            |  |
| Carcinoid tumour of the gastrointestinal tract  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervix carcinoma                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Cholangiocarcinoma                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic lymphocytic leukaemia                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clear cell renal cell carcinoma                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon adenoma                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon cancer                                    |                  |                  |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Colon neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colorectal adenocarcinoma                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colorectal cancer                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diffuse large B-cell lymphoma                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diffuse large B-cell lymphoma stage IV          |                  |                  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Ductal adenocarcinoma of pancreas                    |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Endometrial adenocarcinoma                           |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Endometrial cancer                                   |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Endometrial cancer stage III                         |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Extranodal marginal zone B-cell lymphoma (MALT type) |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Fibroma  |                  |                  |  |
| subjects affected / exposed                          | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Fibrous histiocytoma                                 |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Gallbladder adenocarcinoma                           |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric adenoma                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 1 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 2            |  |
| Gastrointestinal carcinoma                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal tract adenoma                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glioblastoma                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Glioma  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemangioma                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cancer                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hepatic cancer metastatic                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 1 / 2            | 0 / 0            |  |
| Hepatic cancer stage IV                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic neoplasm                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hepatocellular carcinoma                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hodgkin's disease                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypergammaglobulinaemia benign monoclonal       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inflammatory pseudotumour                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal adenocarcinoma                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intraductal proliferative breast lesion         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Invasive breast carcinoma                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Invasive ductal breast carcinoma                |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Keratoacanthoma                                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large intestine benign neoplasm                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngeal cancer                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngeal squamous cell carcinoma               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lentigo maligna                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leukaemia                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lip and/or oral cavity cancer                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lip squamous cell carcinoma                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lipoma  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liposarcoma                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Lung adenocarcinoma                             |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 4            | 0 / 0            |  |
| Lung adenocarcinoma stage III                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung adenocarcinoma stage IV                    |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lung cancer metastatic                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Lung carcinoma cell type unspecified recurrent  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Lung carcinoma cell type unspecified stage III  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lung neoplasm                                   |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 1             |  |
| Lung neoplasm malignant                         |                   |                   |  |
| subjects affected / exposed                     | 25 / 3348 (0.75%) | 14 / 5777 (0.24%) |  |
| occurrences causally related to treatment / all | 3 / 25            | 1 / 14            |  |
| deaths causally related to treatment / all      | 0 / 16            | 1 / 7             |  |
| Lung squamous cell carcinoma metastatic         |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Lymphoma  |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lymphoproliferative disorder                    |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant fibrous histiocytoma                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant mediastinal neoplasm                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Malignant melanoma                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant melanoma in situ                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant neoplasm of pleura                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Malignant neoplasm of unknown primary site      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant peritoneal neoplasm                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant pleural effusion                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Mantle cell lymphoma                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Medullary thyroid cancer                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningioma                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningioma benign                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to adrenals                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to bone                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to central nervous system            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Metastases to kidney                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to liver                             |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 1 / 2            |  |
| deaths causally related to treatment / all      | 1 / 4            | 1 / 1            |  |
| Metastases to lung                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |
| Metastases to lymph nodes                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to pelvis                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to pleura                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to rectum                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to spine                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastatic bronchial carcinoma                  |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastatic malignant melanoma                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastatic renal cell carcinoma                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastatic squamous cell carcinoma              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Monoclonal gammopathy                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mucinous adenocarcinoma of appendix             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mycosis fungoides                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myelodysplastic syndrome                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myelofibrosis                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal cavity cancer                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neoplasm malignant                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 0            |  |
| Neoplasm skin                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuroendocrine breast tumour                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuroendocrine carcinoma                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Non-Hodgkin's lymphoma                          |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-Hodgkin's lymphoma refractory               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-small cell lung cancer                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Non-small cell lung cancer metastatic           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-small cell lung cancer stage IV             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal adenocarcinoma                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Oesophageal adenocarcinoma stage II             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Oesophageal cancer metastatic                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal carcinoma                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Oesophageal neoplasm                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal squamous cell carcinoma             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oligodendroglioma                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oropharyngeal squamous cell carcinoma           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian adenoma                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian neoplasm                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatic carcinoma                            |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 0 / 3            |  |
| deaths causally related to treatment / all      | 1 / 3            | 0 / 2            |  |
| Pancreatic carcinoma metastatic                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 1 / 2            | 0 / 0            |  |
| Papillary cystadenoma lymphomatosum             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Papillary renal cell carcinoma                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Papillary thyroid cancer                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parathyroid tumour benign                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Penile cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Phaeochromocytoma                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pharyngeal cancer                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pituitary tumour benign                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Plasma cell myeloma                             |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pleomorphic adenoma                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Polycythaemia vera                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer                                 |                   |                   |  |
| subjects affected / exposed                     | 13 / 3348 (0.39%) | 15 / 5777 (0.26%) |  |
| occurrences causally related to treatment / all | 1 / 13            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer metastatic                      |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer recurrent                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostatic adenoma                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Rectal adenocarcinoma                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Rectal adenoma                                  |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Rectal cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectosigmoid cancer                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cancer                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Renal cancer metastatic                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Renal cell carcinoma                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Renal neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal oncocytoma                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rosai-Dorfman syndrome                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland adenoma                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland neoplasm                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Seborrhoeic keratosis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin cancer                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small cell lung cancer                          |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 1            |  |
| Small cell lung cancer metastatic               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestine adenocarcinoma                  |                  |                  |  |



|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            |  |
| Small intestine carcinoma                       |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Small intestine carcinoma metastatic            |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Squamous cell carcinoma                         |                   |                  |  |
| subjects affected / exposed                     | 10 / 3348 (0.30%) | 9 / 5777 (0.16%) |  |
| occurrences causally related to treatment / all | 2 / 11            | 1 / 9            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            |  |
| Squamous cell carcinoma of lung                 |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1             | 1 / 1            |  |
| Squamous cell carcinoma of skin                 |                   |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Squamous cell carcinoma of the hypopharynx      |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Squamous cell carcinoma of the tongue           |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Superficial spreading melanoma stage II         |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Testis cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Throat cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroid cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroid cancer metastatic                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroid neoplasm                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tongue neoplasm malignant stage unspecified     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tonsil cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transitional cell carcinoma                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transitional cell carcinoma urethra             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Tumour perforation                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Uterine cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Uterine leiomyoma                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular disorders                              |                  |                  |  |
| Accelerated hypertension                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aneurysm ruptured                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Angiodysplasia                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic aneurysm                                 |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 12 / 5777 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Aortic aneurysm rupture                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2             |  |
| Aortic dissection                               |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Aortic stenosis                                 |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Aortitis  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Arterial haemorrhage                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Arterial insufficiency                          |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Arteriosclerosis                                |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 5 / 5777 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 3             |  |
| Arteriovenous fistula                           |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteritis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brachiocephalic artery stenosis                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Circulatory collapse                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Deep vein thrombosis                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Embolism  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Embolism arterial                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Embolism venous                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Essential hypertension                          |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Extremity necrosis                              |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Femoral artery aneurysm                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Femoral artery embolism                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haematoma                                       |                   |                   |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%)  | 5 / 5777 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haemodynamic instability                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Haemorrhage                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypertension                                    |                   |                   |  |
| subjects affected / exposed                     | 15 / 3348 (0.45%) | 17 / 5777 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 29            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |  |
| Hypertensive crisis                             |                   |                   |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 11 / 3348 (0.33%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 13            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hypertensive emergency                          |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hypotension                                     |                   |                  |  |
| subjects affected / exposed                     | 11 / 3348 (0.33%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hypovolaemic shock                              |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            |  |
| Intermittent claudication                       |                   |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Internal haemorrhage                            |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Ischaemic limb pain                             |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Lymphatic fistula                               |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Lymphorrhoea                                    |                   |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Malignant hypertension                          |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Orthostatic hypertension                        |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Orthostatic hypotension                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pallor  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral arterial occlusive disease           |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 11 / 5777 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral artery aneurysm                      |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral artery occlusion                     |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 4 / 5777 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral artery stenosis                      |                  |                   |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 6 / 5777 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral artery thrombosis                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral embolism                             |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral ischaemia                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 11 / 5777 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Peripheral vascular disorder                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 4 / 5777 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Peripheral venous disease                       |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Shock   |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Shock haemorrhagic                              |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Temporal arteritis                              |                  |                   |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                          | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Thrombophlebitis                                     |                  |                  |  |
| subjects affected / exposed                          | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Thrombophlebitis superficial                         |                  |                  |  |
| subjects affected / exposed                          | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Thrombosis   |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Varicose ulceration                                  |                  |                  |  |
| subjects affected / exposed                          | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Varicose vein  |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Vascular insufficiency                               |                  |                  |  |
| subjects affected / exposed                          | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Venous thrombosis limb                               |                  |                  |  |
| subjects affected / exposed                          | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| General disorders and administration site conditions |                  |                  |  |
| Adverse drug reaction                                |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Asthenia  |                  |                   |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Cardiac death                                   |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 4 / 5777 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 4             |  |
| Chest discomfort                                |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Chest pain                                      |                  |                   |  |
| subjects affected / exposed                     | 9 / 3348 (0.27%) | 9 / 5777 (0.16%)  |  |
| occurrences causally related to treatment / all | 1 / 10           | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Chills  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Complication associated with device             |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Death   |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 12 / 5777 (0.21%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 1 / 12            |  |
| deaths causally related to treatment / all      | 1 / 4            | 1 / 12            |  |
| Drowning  |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Drug intolerance                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Exercise tolerance decreased                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Facial pain                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fatigue   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gait disturbance                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| General physical health deterioration           |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Generalised oedema                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hernia  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Heteroplasia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hyperplasia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypothermia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Impaired healing                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Implant site irritation                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incarcerated hernia                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inflammation                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Influenza like illness                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injection site reaction                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic ulcer                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Local swelling                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malaise   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mass  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Multiple organ dysfunction syndrome             |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 1 / 3            | 0 / 5            |  |
| Necrosis  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-cardiac chest pain                          |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 75 / 3348 (2.24%) | 35 / 5777 (0.61%) |  |
| occurrences causally related to treatment / all | 1 / 92            | 0 / 36            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Oedema peripheral                               |                   |                   |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Pacemaker syndrome                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pain  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Polyp   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pseudocyst                                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pyrexia   |                   |                   |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%)  | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Stent-graft endoleak                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sudden cardiac death                            |                   |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 11 / 5777 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 11            |  |
| Sudden death                                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 7 / 5777 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 7             |  |
| Surgical failure                                |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Systemic inflammatory response syndrome         |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Vascular stent restenosis                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Vascular stent stenosis                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Vascular stent thrombosis                       |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Vessel puncture site haemorrhage                |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Immune system disorders                         |                  |                   |  |
| Allergy to arthropod sting                      |                  |                   |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaphylactic reaction                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaphylactic shock                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Contrast media allergy                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Drug hypersensitivity                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypersensitivity                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Social circumstances                            |                  |                  |  |
| Homicide  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Reproductive system and breast disorders        |                  |                  |  |
| Balanoposthitis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Benign prostatic hyperplasia                    |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 8 / 5777 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystocele                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dysmenorrhoea                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endometrial hyperplasia                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epididymal cyst                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erectile dysfunction                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Female genital tract fistula                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Genital atrophy                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Genital prolapse                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Menorrhagia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian cyst                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic pain                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postmenopausal haemorrhage                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatic haemorrhage                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatic mass                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatism                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatitis                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatomegaly                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectocele                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spermatocele                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Uterine cervix stenosis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Uterine prolapse                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vaginal haemorrhage                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Varicocele                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Varicose veins pelvic                           |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory, thoracic and mediastinal disorders |                   |                   |  |
| Acute pulmonary oedema                          |                   |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Acute respiratory distress syndrome             |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 1 / 1             | 0 / 0             |  |
| Acute respiratory failure                       |                   |                   |  |
| subjects affected / exposed                     | 13 / 3348 (0.39%) | 21 / 5777 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 13            | 0 / 24            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 4             |  |
| Alveolitis                                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Alveolitis allergic                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Asphyxia  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Asthma  |                   |                   |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Atelectasis                                     |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchial hyperreactivity                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchial obstruction                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchiectasis                                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchitis chronic                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchospasm                                    |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cheyne-Stokes respiration                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chronic obstructive pulmonary disease           |                   |                   |  |
| subjects affected / exposed                     | 40 / 3348 (1.19%) | 33 / 5777 (0.57%) |  |
| occurrences causally related to treatment / all | 3 / 54            | 3 / 41            |  |
| deaths causally related to treatment / all      | 0 / 2             | 1 / 3             |  |
| Cough   |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Dyspnoea  |                   |                   |  |
| subjects affected / exposed                     | 23 / 3348 (0.69%) | 19 / 5777 (0.33%) |  |
| occurrences causally related to treatment / all | 0 / 25            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |  |
| Dyspnoea exertional                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Dyspnoea paroxysmal nocturnal                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Emphysema                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Epistaxis                                       |                   |                   |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haemoptysis                                     |                   |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haemothorax                                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hiccups   |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydrothorax                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypopnoea                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxia   |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Idiopathic interstitial pneumonia               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Idiopathic pneumonia syndrome                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Idiopathic pulmonary fibrosis                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Interstitial lung disease                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Laryngeal oedema                                |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngospasm                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung consolidation                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung hernia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung infiltration                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal obstruction                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal polyps                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal turbinate hypertrophy                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Obstructive airways disorder                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Organising pneumonia                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oropharyngeal pain                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pickwickian syndrome                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleural adhesion                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleural effusion                                |                  |                  |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 2 / 7            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleurisy  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleuritic pain                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumomediastinum                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia aspiration                            |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonitis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumothorax                                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumothorax spontaneous                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Productive cough                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary alveolar haemorrhage                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary arterial hypertension                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary congestion                            |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary embolism                              |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 18 / 5777 (0.31%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 2             |  |
| Pulmonary fibrosis                              |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1             |  |
| Pulmonary haematoma                             |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary hypertension                          |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary mass                                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Pulmonary microemboli                           |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pulmonary oedema                                |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 5 / 5777 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2             |  |
| Pulmonary sarcoidosis                           |                  |                   |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Respiratory alkalosis                           |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Respiratory arrest                              |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Respiratory distress                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            |  |
| Respiratory failure                             |                   |                  |  |
| subjects affected / exposed                     | 12 / 3348 (0.36%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 4             | 0 / 1            |  |
| Respiratory tract inflammation                  |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            |  |
| Respiratory tract irritation                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Rhinitis allergic                               |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Sinus congestion                                |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus polyp                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sleep apnoea syndrome                           |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Status asthmaticus                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vocal cord leukoplakia                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wheezing  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psychiatric disorders                           |                  |                  |  |
| Acute stress disorder                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adjustment disorder                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Affective disorder                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                         | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Alcoholic psychosis                                 |                  |                  |  |
| subjects affected / exposed                         | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Alcoholism  |                  |                  |  |
| subjects affected / exposed                         | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Anxiety   |                  |                  |  |
| subjects affected / exposed                         | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all     | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Anxiety disorder                                    |                  |                  |  |
| subjects affected / exposed                         | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Anxiety disorder due to a general medical condition |                  |                  |  |
| subjects affected / exposed                         | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Bipolar I disorder                                  |                  |                  |  |
| subjects affected / exposed                         | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Bipolar disorder                                    |                  |                  |  |
| subjects affected / exposed                         | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all     | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all          | 0 / 0            | 0 / 0            |  |
| Burnout syndrome                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Completed suicide                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Confusional state                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Conversion disorder                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Delirium  |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Delirium tremens                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Depression                                      |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dissociative amnesia                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Drug use disorder                               |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Generalised anxiety disorder                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hallucination, visual                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Head banging                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Homicidal ideation                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Insomnia  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intentional self-injury                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Major depression                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mental status changes                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                           | 6 / 3348 (0.18%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all       | 0 / 8            | 0 / 2            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Panic attack  |                  |                  |  |
| subjects affected / exposed                           | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Personality change                                    |                  |                  |  |
| subjects affected / exposed                           | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 1            | 0 / 0            |  |
| Psychotic disorder                                    |                  |                  |  |
| subjects affected / exposed                           | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Psychotic disorder due to a general medical condition |                  |                  |  |
| subjects affected / exposed                           | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Restlessness  |                  |                  |  |
| subjects affected / exposed                           | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Schizophrenia   |                  |                  |  |
| subjects affected / exposed                           | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Somnambulism  |                  |                  |  |
| subjects affected / exposed                           | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Suicidal ideation                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Suicide attempt                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Product issues                                  |                  |                  |  |
| Device battery issue                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device dislocation                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device end of service                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device failure                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device inappropriate shock delivery             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device issue                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device lead damage                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device lead issue                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device loosening                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device malfunction                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device occlusion                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device signal detection issue                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lead dislodgement                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatobiliary disorders                         |                  |                  |  |
| Acute hepatic failure                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Alcoholic liver disease                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Autoimmune hepatitis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bile duct stenosis                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bile duct stone                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Biliary cirrhosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Biliary colic                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Biliary dilatation                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Biliary fistula                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholangitis                                     |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cholangitis acute                               |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cholecystitis                                   |                   |                  |  |
| subjects affected / exposed                     | 9 / 3348 (0.27%)  | 7 / 5777 (0.12%) |  |
| occurrences causally related to treatment / all | 1 / 9             | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cholecystitis acute                             |                   |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%)  | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cholelithiasis                                  |                   |                  |  |
| subjects affected / exposed                     | 18 / 3348 (0.54%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cholestasis                                     |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Drug-induced liver injury                       |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gallbladder polyp                               |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Haemorrhagic hepatic cyst                       |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cirrhosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic congestion                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic failure                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic function abnormal                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic steatosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic vein thrombosis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis toxic                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatomegaly                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatorenal failure                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hepatosplenomegaly                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydrocholecystis                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic hepatitis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Jaundice cholestatic                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver disorder                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver injury                                    |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-alcoholic fatty liver                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-alcoholic steatohepatitis                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Portal vein thrombosis                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Steatohepatitis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Investigations                                  |                  |                  |  |
| Alanine aminotransferase increased              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anticoagulation drug level above therapeutic    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aspartate aminotransferase increased            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood creatine phosphokinase MB                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| increased                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood creatine phosphokinase increased          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood creatinine increased                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood glucose increased                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood magnesium decreased                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood pressure increased                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blood urine present                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Body mass index decreased                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Central venous pressure increased               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chest X-ray abnormal                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Clostridium test positive                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ejection fraction decreased                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemoglobin decreased                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic enzyme increased                        |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Human metapneumovirus test positive             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Imaging procedure abnormal                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| International normalised ratio decreased        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                               | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| International normalised ratio increased                  |                  |                  |  |
| subjects affected / exposed                               | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| Liver function test abnormal                              |                  |                  |  |
| subjects affected / exposed                               | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all           | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| Liver function test increased                             |                  |                  |  |
| subjects affected / exposed                               | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| N-terminal prohormone brain natriuretic peptide increased |                  |                  |  |
| subjects affected / exposed                               | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| Oxygen saturation decreased                               |                  |                  |  |
| subjects affected / exposed                               | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| Platelet count decreased                                  |                  |                  |  |
| subjects affected / exposed                               | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| Quality of life decreased                                 |                  |                  |  |
| subjects affected / exposed                               | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0            | 0 / 0            |  |
| Scan myocardial perfusion abnormal                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Troponin T increased                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Troponin increased                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Volume blood decreased                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Weight decreased                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Weight increased                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| White blood cell count increased                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injury, poisoning and procedural complications  |                  |                  |  |
| Abdominal injury                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Accident  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Accidental overdose                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acetabulum fracture                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Alcohol poisoning                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Anaemia postoperative                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anastomotic leak                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Animal bite                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ankle fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial injury                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthropod sting                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Asbestosis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone contusion                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain contusion                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac function disturbance postoperative      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Central cord syndrome                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervical vertebral fracture                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chest injury                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clavicle fracture                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Closed globe injury                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Comminuted fracture                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Concussion                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Contusion                                       |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery restenosis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Craniocerebral injury                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dural tear                                      |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epicondylitis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Face injury                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Facial bones fracture                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fall  |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 9 / 5777 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Femoral neck fracture                           |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Femur fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Foot fracture                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Forearm fracture                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Foreign body                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fracture displacement                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gallbladder injury                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal stoma complication             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal stoma necrosis                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gun shot wound                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hand fracture                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Head injury                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hip fracture                                    |                  |                  |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Humerus fracture                                |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incision site haemorrhage                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incision site pain                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incisional hernia                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incisional hernia, obstructive                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injury  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Intentional overdose                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intentional product misuse                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Jaw fracture                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint dislocation                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint injury                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laceration                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ligament injury                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ligament rupture                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ligament sprain                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Limb injury                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Limb traumatic amputation                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lower limb fracture                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar vertebral fracture                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meniscus injury                                 |                  |                  |  |
| subjects affected / exposed                     | 8 / 3348 (0.24%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Multiple fractures                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Multiple injuries                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle contusion                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle strain                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal foreign body                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nerve injury                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Overdose  |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Patella fracture                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral artery restenosis                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periprosthetic fracture                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perirenal haematoma                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumoconiosis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumothorax traumatic                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural complication                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural discharge                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural fever                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural haematoma                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative hernia                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative wound complication                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural complication                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural intestinal perforation               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural pain                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pubis fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radiation mucositis                             |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radius fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rib fracture                                    |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Road traffic accident                           |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 2            |  |
| Scapula fracture                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Scratch   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Seroma  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skeletal injury                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin laceration                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skull fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal column injury                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal compression fracture                     |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal cord injury                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal cord injury cervical                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenic rupture                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stab wound                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sternal fracture                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stress fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subarachnoid haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Subdural haematoma                              |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Subdural haemorrhage                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Tendon injury                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tendon rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thermal burn                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thoracic vertebral fracture                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tibia fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tooth fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxicity to various agents                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tracheal haemorrhage                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic amputation                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic arthritis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic haematoma                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic haemothorax                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic intracranial haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Ulna fracture                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper limb fracture                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary retention postoperative                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft complication                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular pseudoaneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular pseudoaneurysm ruptured                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound dehiscence                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound secretion                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wrist fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congenital, familial and genetic disorders      |                  |                  |  |
| Atrial septal defect                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Branchial cyst                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebrovascular arteriovenous malformation      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic arteriovenous malformation         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| Hereditary haemochromatosis                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hydrocele                                       |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Nonketotic hyperglycinaemia                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Phimosis  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pyloric stenosis                                |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Tracheo-oesophageal fistula                     |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cardiac disorders                               |                  |                   |  |
| Acute coronary syndrome                         |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 14 / 5777 (0.24%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 3             |  |
| Acute left ventricular failure                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Acute myocardial infarction                     |                  |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 3348 (0.21%)  | 71 / 5777 (1.23%) |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 83            |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 2             |  |
| Adams-Stokes syndrome                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Angina pectoris                                 |                   |                   |  |
| subjects affected / exposed                     | 76 / 3348 (2.27%) | 66 / 5777 (1.14%) |  |
| occurrences causally related to treatment / all | 3 / 84            | 0 / 72            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Angina unstable                                 |                   |                   |  |
| subjects affected / exposed                     | 63 / 3348 (1.88%) | 56 / 5777 (0.97%) |  |
| occurrences causally related to treatment / all | 1 / 72            | 0 / 57            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Aortic valve incompetence                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Aortic valve stenosis                           |                   |                   |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arrhythmia                                      |                   |                   |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Arrhythmia supraventricular                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriosclerosis coronary artery                |                   |                   |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Arteriospasm coronary                           |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Atrial fibrillation                             |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 49 / 5777 (0.85%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 1 / 52            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Atrial flutter                                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 6 / 5777 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Atrial tachycardia                              |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Atrial thrombosis                               |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Atrioventricular block                          |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Atrioventricular block complete                 |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 4 / 5777 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Atrioventricular block first degree             |                  |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Atrioventricular block second degree            |                   |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bradyarrhythmia                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bradycardia                                     |                   |                   |  |
| subjects affected / exposed                     | 10 / 3348 (0.30%) | 6 / 5777 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 0             |  |
| Cardiac aneurysm                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac arrest                                  |                   |                   |  |
| subjects affected / exposed                     | 15 / 3348 (0.45%) | 9 / 5777 (0.16%)  |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 6             | 0 / 6             |  |
| Cardiac discomfort                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac failure                                 |                   |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%)  | 43 / 5777 (0.74%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 1 / 54            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 9             |  |
| Cardiac failure acute                           |                   |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 16 / 5777 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Cardiac failure chronic                         |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 15 / 5777 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2             |  |
| Cardiac failure congestive                      |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 30 / 5777 (0.52%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 37            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 3             |  |
| Cardiac fibrillation                            |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cardiac pseudoaneurysm                          |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cardiac tamponade                               |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cardiac ventricular thrombosis                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cardio-respiratory arrest                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 6 / 5777 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 5             |  |
| Cardiogenic shock                               |                  |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 3348 (0.21%)  | 9 / 5777 (0.16%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 1 / 9             |  |
| deaths causally related to treatment / all      | 0 / 4             | 1 / 5             |  |
| Cardiomegaly                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Cardiomyopathy                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiopulmonary failure                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Conduction disorder                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Congestive cardiomyopathy                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cor pulmonale                                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary artery disease                         |                   |                   |  |
| subjects affected / exposed                     | 20 / 3348 (0.60%) | 27 / 5777 (0.47%) |  |
| occurrences causally related to treatment / all | 0 / 29            | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |  |
| Coronary artery insufficiency                   |                   |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Coronary artery occlusion                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Coronary artery stenosis                        |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 14 / 5777 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hypertensive heart disease                      |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Intracardiac thrombus                           |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Ischaemic cardiomyopathy                        |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 6 / 5777 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 1 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 3             |  |
| Left ventricular dysfunction                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Left ventricular failure                        |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Left ventricular hypertrophy                    |                  |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Microvascular coronary artery disease           |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Mitral valve incompetence                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Myocardial infarction                           |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 42 / 5777 (0.73%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 42            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 10            |  |
| Myocardial ischaemia                            |                  |                   |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 10 / 5777 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2             |  |
| Nodal arrhythmia                                |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Palpitations                                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pericardial effusion                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pericarditis                                    |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prinzmetal angina                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulseless electrical activity                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Right ventricular dysfunction                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Right ventricular failure                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Silent myocardial infarction                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus arrest                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus bradycardia                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus node dysfunction                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus tachycardia                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stress cardiomyopathy                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Supraventricular tachycardia                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tachyarrhythmia                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tachycardia                                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Torsade de pointes                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tricuspid valve incompetence                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Trifascicular block                             |                  |                  |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ventricular arrhythmia                          |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Ventricular extrasystoles                       |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ventricular fibrillation                        |                   |                   |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%)  | 7 / 5777 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 3             |  |
| Ventricular tachyarrhythmia                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ventricular tachycardia                         |                   |                   |  |
| subjects affected / exposed                     | 16 / 3348 (0.48%) | 18 / 5777 (0.31%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Nervous system disorders                        |                   |                   |  |
| Amnesia   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Amyotrophic lateral sclerosis                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Aphasia   |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Apraxia   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ataxia  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Balance disorder                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain injury                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain oedema                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Carotid arteriosclerosis                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid artery aneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid artery disease                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid artery occlusion                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid artery stenosis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 8 / 5777 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 12           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carpal tunnel syndrome                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cauda equina syndrome                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebellar infarction                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebellar stroke                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral arteriosclerosis                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral haemorrhage                            |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cerebral infarction                             |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 9 / 5777 (0.16%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cerebral ischaemia                              |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Cerebrovascular accident                        |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 22 / 5777 (0.38%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cervical myelopathy                             |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cervical radiculopathy                          |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cervicobrachial syndrome                        |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cognitive disorder                              |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Coma  |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dementia  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Dementia Alzheimer's type                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dementia with Lewy bodies                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Depressed level of consciousness                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic coma                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic neuropathy                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diplegia  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dizziness                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dysaesthesia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dysarthria                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dystonia  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Embololic stroke                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encephalopathy                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Epilepsy  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Facial paralysis                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Focal dyscognitive seizures                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Generalised tonic-clonic seizure                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Guillain-Barre syndrome                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhage intracranial                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Haemorrhagic stroke                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic transformation stroke              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Headache  |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hemiparesis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hydrocephalus                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypersomnia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertensive encephalopathy                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoaesthesia                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemic coma                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemic encephalopathy                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxic-ischaemic encephalopathy                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| IIIrd nerve paresis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intracranial aneurysm                           |                  |                  |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Intracranial pressure increased                 |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Ischaemic stroke                                |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 16 / 5777 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Lacunar infarction                              |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lacunar stroke                                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Loss of consciousness                           |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lumbar radiculopathy                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lumbosacral radiculopathy                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Mental impairment                               |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolic encephalopathy                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Migraine  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mixed dementia                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nerve compression                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuralgia                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuropathy peripheral                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Normal pressure hydrocephalus                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Optic neuritis                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Orthostatic intolerance                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paraesthesia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paralysis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Paresis   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Partial seizures                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral nerve lesion                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polyneuropathy                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post herpetic neuralgia                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post stroke seizure                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Presyncope                                      |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Restless legs syndrome                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sciatica  |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Seizure   |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sensory disturbance                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal claudication                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal cord compression                         |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spinal cord infarction                          |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 1 / 1             | 0 / 0             |  |
| Spondylitic myelopathy                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Status epilepticus                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Stupor  |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Subdural hygroma                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Syncope   |                   |                   |  |
| subjects affected / exposed                     | 25 / 3348 (0.75%) | 16 / 5777 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 27            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tension headache                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Thalamic infarction                             |                   |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Thrombotic cerebral infarction                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Tonic convulsion                                |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Toxic encephalopathy                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Transient global amnesia                        |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Transient ischaemic attack                      |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 15 / 5777 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Trigeminal neuralgia                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Upper motor neurone lesion                      |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| VIth nerve paralysis                            |                  |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vascular dementia                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vascular encephalopathy                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vertebrobasilar insufficiency                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood and lymphatic system disorders            |                   |                   |  |
| Abnormal clotting factor                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Anaemia   |                   |                   |  |
| subjects affected / exposed                     | 14 / 3348 (0.42%) | 10 / 5777 (0.17%) |  |
| occurrences causally related to treatment / all | 1 / 15            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Bone marrow oedema                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coagulopathy                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Disseminated intravascular coagulation          |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Febrile neutropenia                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic anaemia                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Heparin-induced thrombocytopenia                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hilar lymphadenopathy                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Histiocytosis haematophagic                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypochromic anaemia                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Immune thrombocytopenic purpura                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Iron deficiency anaemia                         |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leukocytosis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leukopenia                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphadenitis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphadenopathy                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphadenopathy mediastinal                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Microcytic anaemia                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Monoclonal B-cell lymphocytosis                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Normochromic normocytic anaemia                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Normocytic anaemia                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancytopenia                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polycythaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenic infarction                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenomegaly                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombocytopenia                                |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Thrombocytopenic purpura                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ear and labyrinth disorders                     |                  |                  |  |
| Cerumen impaction                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ear pain  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoacusis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meniere's disease                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otosclerosis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Presbycusis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sudden hearing loss                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tympanic membrane perforation                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vertigo   |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 4 / 3348 (0.12%)  | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vertigo positional                              |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Eye disorders                                   |                   |                  |  |
| Amaurosis fugax                                 |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Angle closure glaucoma                          |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Blindness                                       |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 3 / 3             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Blindness transient                             |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Blindness unilateral                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cataract  |                   |                  |  |
| subjects affected / exposed                     | 12 / 3348 (0.36%) | 8 / 5777 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cataract cortical                               |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cataract diabetic                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cataract nuclear                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Corneal degeneration                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Corneal infiltrates                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dacryostenosis acquired                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic retinopathy                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eye haemorrhage                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eyelid ptosis                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glaucoma  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Iridocyclitis                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lens dislocation                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Macular degeneration                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Macular fibrosis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Macular hole                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Macular oedema                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neovascular age-related macular degeneration    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ocular ischaemic syndrome                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Papilloedema                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retinal artery thrombosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retinal detachment                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retinal haemorrhage                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retinal vein occlusion                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retinal vein thrombosis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vitreous haemorrhage                            |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrointestinal disorders                      |                   |                  |  |
| Abdominal adhesions                             |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal discomfort                            |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal distension                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            |  |
| Abdominal hernia                                |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal pain                                  |                   |                  |  |
| subjects affected / exposed                     | 10 / 3348 (0.30%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 11            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            |  |
| Abdominal pain lower                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Abdominal pain upper                            |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Acute abdomen                                   |                   |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Alcoholic pancreatitis                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal fissure                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal haemorrhage                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal skin tags                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal ulcer                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal ulcer haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anorectal disorder                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendiceal mucocoele                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendix disorder                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ascites   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Change of bowel habit                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic gastritis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis   |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 2 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis ischaemic                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis microscopic                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis ulcerative                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colonic fistula                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Constipation                                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Crohn's disease                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dental caries                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic gastroenteropathy                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diarrhoea                                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dieulafoy's vascular malformation               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum intestinal                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum intestinal haemorrhagic            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal ulcer                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Duodenal ulcer haemorrhage                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal ulcer perforation                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenitis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dyspepsia                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dysphagia                                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enteritis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterovesical fistula                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epigastric discomfort                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erosive duodenitis                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erosive oesophagitis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Faecaloma                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Faeces discoloured                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Flatulence                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Food poisoning                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gallstone ileus                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric haemorrhage                             |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric ulcer                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric ulcer haemorrhage                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric ulcer perforation                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric volvulus                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis                                       |                  |                  |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis erosive                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis haemorrhagic                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroduodenitis                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal angiodysplasia                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal disorder                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal erosion                        |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrointestinal haemorrhage                    |                   |                  |  |
| subjects affected / exposed                     | 13 / 3348 (0.39%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            |  |
| Gastrointestinal necrosis                       |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrointestinal pain                           |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrointestinal perforation                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            |  |
| Gastrointestinal ulcer                          |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrointestinal vascular malformation          |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrooesophageal reflux disease                |                   |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%)  | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Haematemesis                                    |                   |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematochezia                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic necrotic pancreatitis              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoidal haemorrhage                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoids                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoids thrombosed                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hiatus hernia                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileal ulcer                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileus   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileus paralytic                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Impaired gastric emptying                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incarcerated inguinal hernia                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incarcerated umbilical hernia                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inflammatory bowel disease                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inguinal hernia                                 |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 8 / 5777 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inguinal hernia strangulated                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal fistula                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal infarction                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal ischaemia                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Intestinal mass                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal obstruction                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Intestinal perforation                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal ulcer                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Irritable bowel syndrome                        |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Ischaemic enteritis                             |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Large intestinal obstruction                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Large intestinal stenosis                       |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Large intestine perforation                     |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Large intestine polyp                           |                   |                  |  |
| subjects affected / exposed                     | 12 / 3348 (0.36%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 13            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Lower gastrointestinal haemorrhage              |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Mallory-Weiss syndrome                          |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Melaena   |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesenteric artery stenosis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesenteric artery thrombosis                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesenteric vascular insufficiency               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mouth cyst                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mouth ulceration                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Narcotic bowel syndrome                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nausea  |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Obstruction gastric                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Odynophagia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal obstruction                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal perforation                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal rupture                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal stenosis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal ulcer                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal varices haemorrhage                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Oesophagitis                                    |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pancreatic cyst                                 |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pancreatic disorder                             |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pancreatic duct dilatation                      |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pancreatic mass                                 |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pancreatic pseudocyst                           |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pancreatitis                                    |                   |                  |  |
| subjects affected / exposed                     | 11 / 3348 (0.33%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 1 / 13            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1            |  |
| Pancreatitis acute                              |                   |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 2 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pancreatitis chronic                            |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatitis necrotising                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peptic ulcer                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peptic ulcer haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritoneal haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumatosis intestinalis                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumoperitoneum                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Proctalgia                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Proctitis                                       |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ranula  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal haemorrhage                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal lesion                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal perforation                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal polyp                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal haematoma                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland calculus                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestinal haemorrhage                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestinal obstruction                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 9 / 5777 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Small intestinal perforation                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestine ulcer                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subileus  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombosis mesenteric vessel                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Umbilical hernia                                |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper gastrointestinal haemorrhage              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 8 / 3348 (0.24%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Vomiting  |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin and subcutaneous tissue disorders          |                  |                  |  |
| Acne  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Actinic keratosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Angioedema                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blister   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brow ptosis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Decubitus ulcer                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dermatitis                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dermatitis allergic                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic foot                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eczema  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erythema  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperhidrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperkeratosis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypersensitivity vasculitis                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neurodermatitis                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prurigo   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pruritus allergic                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psoriasis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rhinophyma                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin ulcer                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stasis dermatitis                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stevens-Johnson syndrome                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subcutaneous emphysema                          |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urticaria                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal and urinary disorders                     |                   |                   |  |
| Acute kidney injury                             |                   |                   |  |
| subjects affected / exposed                     | 27 / 3348 (0.81%) | 22 / 5777 (0.38%) |  |
| occurrences causally related to treatment / all | 3 / 29            | 1 / 25            |  |
| deaths causally related to treatment / all      | 1 / 1             | 0 / 0             |  |
| Acute prerenal failure                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Anuria  |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Azotaemia                                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Calculus bladder                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 3 / 5777 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Calculus urethral                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Calculus urinary                                |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic kidney disease                          |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 2            |  |
| Diabetic nephropathy                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dysuria   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| End stage renal disease                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Focal segmental glomerulosclerosis              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glomerulonephritis membranous                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematuria                                      |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydronephrosis                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertensive nephropathy                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lower urinary tract symptoms                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrolithiasis                                 |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrotic syndrome                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Obstructive uropathy                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pollakiuria                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polyuria  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prerenal failure                                |                  |                  |  |



|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Renal artery stenosis                           |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Renal artery thrombosis                         |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Renal colic                                     |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Renal cyst                                      |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Renal failure                                   |                   |                  |  |
| subjects affected / exposed                     | 13 / 3348 (0.39%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 4             | 0 / 0            |  |
| Renal haematoma                                 |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Renal impairment                                |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Renal injury                                    |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal mass                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal tubular necrosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stress urinary incontinence                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tubulointerstitial nephritis                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureteric obstruction                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureteric stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureterolithiasis                                |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urethral obstruction                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary bladder haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary bladder polyp                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary incontinence                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary retention                               |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary tract obstruction                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vesicocutaneous fistula                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocrine disorders                             |                  |                  |  |
| Goitre  |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperparathyroidism primary                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperthyroidism                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypopituitarism                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypothyroidism                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inappropriate antidiuretic hormone secretion    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Primary hyperaldosteronism                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxic goitre                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal and connective tissue disorders |                  |                  |  |
| Arthralgia                                      |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis reactive                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthropathy                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Back pain                                       |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone pain                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bursitis  |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervical spinal stenosis                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chondromalacia                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chondropathy                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Compartment syndrome                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Costochondritis                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dactylitis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dupuytren's contracture                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Exostosis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fasciitis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Finger deformity                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Flank pain                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Foot deformity                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fracture malunion                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gouty arthritis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gouty tophus                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Groin pain                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemarthrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Immunoglobulin G4 related disease               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral disc calcification               |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intervertebral disc compression                 |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intervertebral disc degeneration                |                   |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intervertebral disc disorder                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intervertebral disc displacement                |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intervertebral disc protrusion                  |                   |                  |  |
| subjects affected / exposed                     | 10 / 3348 (0.30%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Jaw cyst  |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Joint instability                               |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Joint swelling                                  |                   |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar spinal stenosis                          |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 5 / 5777 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meniscal degeneration                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metatarsalgia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle atrophy                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle haemorrhage                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle spasms                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle swelling                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscular weakness                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal chest pain                      |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal pain                            |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myalgia   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myofascial pain syndrome                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neck pain                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuropathic arthropathy                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteitis  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteoarthritis                                  |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 51 / 3348 (1.52%) | 26 / 5777 (0.45%) |  |
| occurrences causally related to treatment / all | 0 / 53            | 0 / 27            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteochondrosis                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteolysis                                      |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteonecrosis                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteoporosis                                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteoporotic fracture                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pain in extremity                               |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pain in jaw                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pathological fracture                           |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polyarthritis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polymyalgia rheumatica                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rhabdomyolysis                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rheumatoid arthritis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rotator cuff syndrome                           |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shoulder deformity                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Soft tissue mass                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal column stenosis                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal deformity                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal osteoarthritis                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal pain                                     |                  |                  |  |
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spondylitis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spondylolisthesis                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Synovial cyst                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Synovitis                                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tendonitis                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tenosynovitis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Trigger finger                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vertebral foraminal stenosis                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vertebral wedging                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| Abdominal abscess                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal infection                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess intestinal                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess jaw                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess limb                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess neck                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0            |  |
| Abscess oral                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess soft tissue                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute hepatitis B                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute sinusitis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal abscess                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendicitis                                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendicitis perforated                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis bacterial                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis infective                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atypical pneumonia                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacteraemia                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial disease carrier                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial pyelonephritis                        |                  |                  |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Bacterial sepsis</b>                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Bacteroides infection</b>                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Bartholin's abscess</b>                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Beta haemolytic streptococcal infection</b>  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Bone abscess</b>                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| <b>Bronchitis</b>                               |                   |                   |  |
| subjects affected / exposed                     | 14 / 3348 (0.42%) | 10 / 5777 (0.17%) |  |
| occurrences causally related to treatment / all | 1 / 14            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| <b>Bronchitis bacterial</b>                     |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| <b>Bursitis infective</b>                       |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bursitis infective staphylococcal               |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Campylobacter gastroenteritis                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Campylobacter infection                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Candida infection                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Carbuncle                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cellulitis                                      |                   |                   |  |
| subjects affected / exposed                     | 27 / 3348 (0.81%) | 22 / 5777 (0.38%) |  |
| occurrences causally related to treatment / all | 4 / 29            | 2 / 22            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |  |
| Cellulitis gangrenous                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cellulitis of male external genital organ       |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cellulitis staphylococcal                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Central nervous system infection                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chikungunya virus infection                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholangitis infective                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholecystitis infective                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chorioretinitis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic sinusitis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic tonsillitis                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridial infection                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridium difficile colitis                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridium difficile infection                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colonic abscess                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Conjunctivitis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Corona virus infection                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Creutzfeldt-Jakob disease                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Cystitis  |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Dengue fever                                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Device related infection                        |                   |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 4             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0            |  |
| Device related sepsis                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic foot infection                         |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic gangrene                               |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diarrhoea infectious                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diverticulitis                                  |                   |                  |  |
| subjects affected / exposed                     | 13 / 3348 (0.39%) | 6 / 5777 (0.10%) |  |
| occurrences causally related to treatment / all | 3 / 15            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Ear infection                                   |                   |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Empyema   |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Endocarditis                                    |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Endocarditis bacterial                          |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Enteritis infectious                            |                  |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Epididymitis                                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Epiglottitis                                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Erysipelas                                      |                  |                   |  |
| subjects affected / exposed                     | 9 / 3348 (0.27%) | 13 / 5777 (0.23%) |  |
| occurrences causally related to treatment / all | 2 / 9            | 2 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Escherichia sepsis                              |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia urinary tract infection             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| External ear cellulitis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Folliculitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fungal skin infection                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Furuncle  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gallbladder abscess                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gallbladder empyema                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gangrene  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis viral                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis                                 |                  |                  |  |
| subjects affected / exposed                     | 8 / 3348 (0.24%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 1 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis clostridial                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis rotavirus                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis salmonella                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis viral                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal bacterial infection            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal infection                      |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal viral infection                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Groin infection                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematoma infection                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemophilus infection                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemophilus sepsis                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic pneumonia                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Helicobacter infection                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic amoebiasis                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis viral                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes ophthalmic                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster                                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 2 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Human ehrlichiosis                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypopyon  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Implant site abscess                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Implant site infection                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incision site cellulitis                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Incision site infection                                       |                  |                  |  |
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infected bite   |                  |                  |  |
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infected cyst   |                  |                  |  |
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infected skin ulcer   |                  |                  |  |
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infection   |                  |                  |  |
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infectious colitis  |                  |                  |  |
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infectious pleural effusion                                   |                  |                  |  |
| subjects affected / exposed                                   | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infective exacerbation of chronic obstructive airways disease |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infective spondylitis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Influenza                                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 9 / 5777 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 2 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 3            |  |
| Intervertebral discitis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Labyrinthitis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leptospirosis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Localised infection                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Lower respiratory tract infection               |                  |                  |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 3 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung abscess                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung infection                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lyme disease                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphangitis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malaria   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mastoiditis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mediastinitis                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Medical device site infection                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningitis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningitis bacterial                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Meningococcal sepsis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesenteric abscess                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metapneumovirus infection                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle abscess                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mycobacterial infection                         |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Mycobacterium avium complex infection           |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Necrotising fasciitis                           |                  |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Neutropenic sepsis                              |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Oesophageal candidiasis                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Orchitis  |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Osteomyelitis                                   |                  |                   |  |
| subjects affected / exposed                     | 4 / 3348 (0.12%) | 10 / 5777 (0.17%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 2 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Osteomyelitis bacterial                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Osteomyelitis blastomyces                       |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis externa                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media acute                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media chronic                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatic abscess                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parainfluenzae virus infection                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parametritis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paronychia                                      |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parotitis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic abscess                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perichondritis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perineal abscess                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periodontitis                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periorbital cellulitis                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perirectal abscess                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritoneal abscess                              |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peritonitis                                     |                   |                   |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Pharyngeal abscess                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pharyngitis                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pharyngitis streptococcal                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pilonidal cyst                                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pneumococcal sepsis                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pneumonia                                       |                   |                   |  |
| subjects affected / exposed                     | 83 / 3348 (2.48%) | 70 / 5777 (1.21%) |  |
| occurrences causally related to treatment / all | 17 / 95           | 10 / 73           |  |
| deaths causally related to treatment / all      | 1 / 5             | 1 / 5             |  |
| Pneumonia bacterial                             |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia escherichia                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia haemophilus                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia klebsiella                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 1            |  |
| Pneumonia legionella                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia necrotising                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia pneumococcal                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pneumonia pseudomonal                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia staphylococcal                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural cellulitis                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural infection                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural sepsis                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative abscess                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative wound infection                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Proctitis infectious                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Propionibacterium infection                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pseudomembranous colitis                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pseudomonal bacteraemia                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pseudomonas bronchitis                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pseudomonas infection                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psoas abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 2            |  |
| Pulmonary tuberculosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyelitis  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyelonephritis                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 3348 (0.15%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyelonephritis acute                            |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyoderma  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyuria  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory tract infection                     |                  |                  |  |
| subjects affected / exposed                     | 7 / 3348 (0.21%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 3 / 8            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory tract infection viral               |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rhinitis  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rubella   |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Salmonellosis                                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Scrotal abscess                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Scrub typhus                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 2 / 5777 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sepsis  |                   |                   |  |
| subjects affected / exposed                     | 19 / 3348 (0.57%) | 22 / 5777 (0.38%) |  |
| occurrences causally related to treatment / all | 5 / 21            | 3 / 22            |  |
| deaths causally related to treatment / all      | 4 / 8             | 0 / 5             |  |
| Sepsis syndrome                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Septic embolus                                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Septic necrosis                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Septic shock                                    |                   |                   |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 11 / 3348 (0.33%) | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 1 / 11            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 7             | 0 / 2            |  |
| Sialoadenitis                                   |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Sinusitis                                       |                   |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%)  | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Sinusitis fungal                                |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Staphylococcal abscess                          |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Staphylococcal bacteraemia                      |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 3 / 5777 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Staphylococcal infection                        |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Staphylococcal mediastinitis                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Staphylococcal sepsis                           |                   |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Streptococcal bacteraemia                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Streptococcal sepsis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subcutaneous abscess                            |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subdiaphragmatic abscess                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subdural empyema                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Testicular abscess                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tetanus   |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Tonsillitis                                     |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tooth abscess                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tracheobronchitis                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 1 / 5777 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Tuberculosis                                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Upper respiratory tract infection               |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection                         |                   |                   |  |
| subjects affected / exposed                     | 21 / 3348 (0.63%) | 19 / 5777 (0.33%) |  |
| occurrences causally related to treatment / all | 3 / 24            | 4 / 20            |  |
| deaths causally related to treatment / all      | 0 / 2             | 1 / 1             |  |
| Urinary tract infection bacterial               |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection enterococcal            |                   |                   |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection fungal                  |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary tract infection pseudomonal             |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urosepsis                                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 7 / 5777 (0.12%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 1 / 7            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Vestibular neuronitis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral cardiomyopathy                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral diarrhoea                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral infection                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral upper respiratory tract infection         |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vulval abscess                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound infection                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound infection bacterial                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound infection staphylococcal                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound sepsis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolism and nutrition disorders              |                  |                  |  |
| Acidosis  |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cachexia  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dehydration                                     |                  |                  |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 8 / 5777 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetes mellitus                               |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 11 / 3348 (0.33%) | 8 / 5777 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1            |  |
| Diabetes mellitus inadequate control            |                   |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetes with hyperosmolarity                   |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic complication                           |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic ketoacidosis                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic metabolic decompensation               |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 2 / 5777 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Electrolyte imbalance                           |                   |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%)  | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Fluid overload                                  |                   |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%)  | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gout  |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperammonaemia                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypercalcaemia                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperchloraemia                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperglycaemia                                  |                  |                  |  |
| subjects affected / exposed                     | 6 / 3348 (0.18%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hyperglycaemic hyperosmolar nonketotic syndrome |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperkalaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 3348 (0.09%) | 7 / 5777 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypermagnesaemia                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperuricaemia                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoalbuminaemia                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypocalcaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 9 / 3348 (0.27%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 12           | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypokalaemia                                    |                  |                  |  |
| subjects affected / exposed                     | 9 / 3348 (0.27%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 11           | 1 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypomagnesaemia                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyponatraemia                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypovolaemia                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Insulin resistant diabetes                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Insulin-requiring type 2 diabetes mellitus      |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ketoacidosis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lactic acidosis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malnutrition                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 1 / 5777 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolic acidosis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Obesity   |                  |                  |  |
| subjects affected / exposed                     | 2 / 3348 (0.06%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Type 1 diabetes mellitus                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 3348 (0.00%) | 0 / 5777 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Type 2 diabetes mellitus                        |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 3348 (0.03%) | 4 / 5777 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Group I              | Group II             | Group III            |
|---|----------------------|----------------------|----------------------|
| Total subjects affected by non-serious adverse events |                      |                      |                      |
| subjects affected / exposed                           | 1271 / 2263 (56.16%) | 1324 / 2285 (57.94%) | 1199 / 2170 (55.25%) |
| Vascular disorders                                    |                      |                      |                      |
| Hypertension  |                      |                      |                      |
| subjects affected / exposed                           | 198 / 2263 (8.75%)   | 216 / 2285 (9.45%)   | 208 / 2170 (9.59%)   |
| occurrences (all)                                     | 242                  | 258                  | 249                  |
| Cardiac disorders                                     |                      |                      |                      |
| Angina pectoris                                       |                      |                      |                      |
| subjects affected / exposed                           | 142 / 2263 (6.27%)   | 164 / 2285 (7.18%)   | 129 / 2170 (5.94%)   |
| occurrences (all)                                     | 176                  | 202                  | 166                  |
| Nervous system disorders                              |                      |                      |                      |
| Dizziness   |                      |                      |                      |
| subjects affected / exposed                           | 114 / 2263 (5.04%)   | 126 / 2285 (5.51%)   | 132 / 2170 (6.08%)   |
| occurrences (all)                                     | 132                  | 148                  | 157                  |
| Headache  |                      |                      |                      |
| subjects affected / exposed                           | 133 / 2263 (5.88%)   | 111 / 2285 (4.86%)   | 120 / 2170 (5.53%)   |
| occurrences (all)                                     | 163                  | 139                  | 183                  |
| General disorders and administration site conditions  |                      |                      |                      |
| Fatigue   |                      |                      |                      |
| subjects affected / exposed                           | 113 / 2263 (4.99%)   | 99 / 2285 (4.33%)    | 84 / 2170 (3.87%)    |
| occurrences (all)                                     | 126                  | 116                  | 91                   |
| Non-cardiac chest pain                                |                      |                      |                      |
| subjects affected / exposed                           | 142 / 2263 (6.27%)   | 143 / 2285 (6.26%)   | 111 / 2170 (5.12%)   |
| occurrences (all)                                     | 172                  | 169                  | 137                  |
| Oedema peripheral                                     |                      |                      |                      |
| subjects affected / exposed                           | 136 / 2263 (6.01%)   | 142 / 2285 (6.21%)   | 134 / 2170 (6.18%)   |
| occurrences (all)                                     | 156                  | 161                  | 153                  |
| Gastrointestinal disorders                            |                      |                      |                      |

|   |   |   |  |
|---|---|---|--|
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 138 / 2263 (6.10%)<br>178   | 146 / 2285 (6.39%)<br>194   | 137 / 2170 (6.31%)<br>201  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)  | <br>151 / 2263 (6.67%)<br>187<br><br>126 / 2263 (5.57%)<br>143  | <br>152 / 2285 (6.65%)<br>171<br><br>123 / 2285 (5.38%)<br>140  | <br>121 / 2170 (5.58%)<br>135<br><br>110 / 2170 (5.07%)<br>133   |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Back pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | <br>165 / 2263 (7.29%)<br>199<br><br>169 / 2263 (7.47%)<br>197<br><br>145 / 2263 (6.41%)<br>171   | <br>181 / 2285 (7.92%)<br>226<br><br>177 / 2285 (7.75%)<br>200<br><br>145 / 2285 (6.35%)<br>166   | <br>144 / 2170 (6.64%)<br>169<br><br>157 / 2170 (7.24%)<br>171<br><br>98 / 2170 (4.52%)<br>114   |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Influenza<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)<br><br>Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | <br>131 / 2263 (5.79%)<br>164<br><br>141 / 2263 (6.23%)<br>168<br><br>153 / 2263 (6.76%)<br>214<br><br>126 / 2263 (5.57%)<br>175<br><br>264 / 2263<br>(11.67%)<br>428 | <br>162 / 2285 (7.09%)<br>204<br><br>145 / 2285 (6.35%)<br>167<br><br>156 / 2285 (6.83%)<br>214<br><br>129 / 2285 (5.65%)<br>194<br><br>297 / 2285<br>(13.00%)<br>477 | <br>114 / 2170 (5.25%)<br>151<br><br>118 / 2170 (5.44%)<br>147<br><br>134 / 2170 (6.18%)<br>189<br><br>93 / 2170 (4.29%)<br>130<br><br>263 / 2170<br>(12.12%)<br>439 |

| <b>Non-serious adverse events</b>                     | Group IV                | Group V                 |  |
|---|-------------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events |                         |                         |  |
| subjects affected / exposed                           | 1905 / 3348<br>(56.90%) | 1497 / 5777<br>(25.91%) |  |
| Vascular disorders                                    |                         |                         |  |
| Hypertension  |                         |                         |  |
| subjects affected / exposed                           | 309 / 3348 (9.23%)      | 241 / 5777 (4.17%)      |  |
| occurrences (all)                                     | 386                     | 261                     |  |
| Cardiac disorders                                     |                         |                         |  |
| Angina pectoris                                       |                         |                         |  |
| subjects affected / exposed                           | 228 / 3348 (6.81%)      | 115 / 5777 (1.99%)      |  |
| occurrences (all)                                     | 284                     | 126                     |  |
| Nervous system disorders                              |                         |                         |  |
| Dizziness   |                         |                         |  |
| subjects affected / exposed                           | 189 / 3348 (5.65%)      | 107 / 5777 (1.85%)      |  |
| occurrences (all)                                     | 223                     | 122                     |  |
| Headache  |                         |                         |  |
| subjects affected / exposed                           | 178 / 3348 (5.32%)      | 72 / 5777 (1.25%)       |  |
| occurrences (all)                                     | 245                     | 85                      |  |
| General disorders and administration site conditions  |                         |                         |  |
| Fatigue   |                         |                         |  |
| subjects affected / exposed                           | 169 / 3348 (5.05%)      | 72 / 5777 (1.25%)       |  |
| occurrences (all)                                     | 191                     | 76                      |  |
| Non-cardiac chest pain                                |                         |                         |  |
| subjects affected / exposed                           | 228 / 3348 (6.81%)      | 68 / 5777 (1.18%)       |  |
| occurrences (all)                                     | 284                     | 71                      |  |
| Oedema peripheral                                     |                         |                         |  |
| subjects affected / exposed                           | 173 / 3348 (5.17%)      | 110 / 5777 (1.90%)      |  |
| occurrences (all)                                     | 196                     | 117                     |  |
| Gastrointestinal disorders                            |                         |                         |  |
| Diarrhoea   |                         |                         |  |
| subjects affected / exposed                           | 216 / 3348 (6.45%)      | 110 / 5777 (1.90%)      |  |
| occurrences (all)                                     | 277                     | 127                     |  |
| Respiratory, thoracic and mediastinal disorders       |                         |                         |  |
| Cough   |                         |                         |  |
| subjects affected / exposed                           | 233 / 3348 (6.96%)      | 103 / 5777 (1.78%)      |  |
| occurrences (all)                                     | 288                     | 115                     |  |

|   |                            |                           |  |
|---|----------------------------|---------------------------|--|
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)                                | 193 / 3348 (5.76%)<br>219  | 112 / 5777 (1.94%)<br>121 |  |
| Musculoskeletal and connective tissue disorders   |                            |                           |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                              | 252 / 3348 (7.53%)<br>297  | 184 / 5777 (3.19%)<br>200 |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                               | 277 / 3348 (8.27%)<br>327  | 163 / 5777 (2.82%)<br>169 |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)                       | 204 / 3348 (6.09%)<br>242  | 128 / 5777 (2.22%)<br>139 |  |
| Infections and infestations   |                            |                           |  |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                              | 234 / 3348 (6.99%)<br>322  | 160 / 5777 (2.77%)<br>183 |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                               | 194 / 3348 (5.79%)<br>248  | 154 / 5777 (2.67%)<br>163 |  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 252 / 3348 (7.53%)<br>343  | 125 / 5777 (2.16%)<br>158 |  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                 | 175 / 3348 (5.23%)<br>247  | 123 / 5777 (2.13%)<br>145 |  |
| Viral upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 388 / 3348 (11.59%)<br>641 | 16 / 5777 (0.28%)<br>16   |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                               |
|-------------------|---|
| 13 September 2016 | Amendment #9 to add the Extension Phase |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Comparison across groups is no longer feasible in the Extension phase because all patients received canakinumab 150 mg. Beyond the primary endpoint, all p-values for the canakinumab 50 mg and 300 mg groups are to be considered nominal only.

Notes: