



## Clinical trial results:

**Effect of ivabradine in patients with stable coronary artery disease without clinical heart failure. A randomised double-blind placebo-controlled international multicentre study.**

**Study assessinG the morbi-mortality beNefits of the If inhibitor ivabradine in patients with coronary arterY disease (SIGNIFY).**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

|                          |                                                             |
|--------------------------|-------------------------------------------------------------|
| EudraCT number           | 2009-011360-10                                              |
| Trial protocol           | ES PT GB NL FI LV HU CZ SK IE BE FR LT DE AT SE IT GR EE SI |
| Global end of trial date | <del>24 January 2014</del><br>24 January 2014               |

## Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v2 (current) |
| This version publication date  | 22 July 2016 |
| First version publication date | 31 July 2015 |

|                         |                                                                                                                                          |
|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| Version creation reason | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Data correction due to a system error in EudraCT – Results |
|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------|

## Trial information

### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CL3-16257-083 |
|-----------------------|---------------|

### Additional study identifiers

|                                    |                |
|------------------------------------|----------------|
| ISRCTN number                      | ISRCTN61576291 |
| ClinicalTrials.gov id (NCT number) | -              |
| WHO universal trial number (UTN)   | -              |

Notes:

## Sponsors

|                              |                                                                                                                                                                    |
|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Institut de Recherches Internationales Servier                                                                                                                     |
| Sponsor organisation address | 50 rue Carnot, Suresnes Cedex, France, 92284                                                                                                                       |
| Public contact               | Therapeutic Innovation Pole, Institut de Recherches Internationales Servier<br>50 rue Carnot<br>92284 Suresnes Cedex, +33 155724366,<br>clinicaltrials@servier.com |
| Scientific contact           | Therapeutic Innovation Pole, Institut de Recherches Internationales Servier<br>50 rue Carnot<br>92284 Suresnes Cedex, +33 155724366,<br>clinicaltrials@servier.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                       | 24 January 2014 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 24 January 2014 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 24 January 2014 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the superiority of ivabradine over placebo in the reduction of CV mortality or non-fatal myocardial infarction.

Protection of trial subjects:

Reason to discontinue the study treatment: study drug not tolerated, no longer appropriate or considered as contra-indicated.

The measurement of drug concentrations in blood was planned in the case of suspected overdose.

Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 25 September 2009 |
| 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 | Korea, Republic of: 446                         |
| Country: Number of subjects enrolled | Kazakhstan: 141                                 |
| Country: Number of subjects enrolled | Latvia: 440                                     |
| Country: Number of subjects enrolled | Lithuania: 302                                  |
| Country: Number of subjects enrolled | Macedonia, the former Yugoslav Republic of: 224 |
| Country: Number of subjects enrolled | Malaysia: 74                                    |
| Country: Number of subjects enrolled | Mexico: 559                                     |
| Country: Number of subjects enrolled | Netherlands: 555                                |
| Country: Number of subjects enrolled | Norway: 56                                      |
| Country: Number of subjects enrolled | Philippines: 30                                 |
| Country: Number of subjects enrolled | Poland: 1157                                    |

|                                      |                          |
|--------------------------------------|--------------------------|
| Country: Number of subjects enrolled | Portugal: 27             |
| Country: Number of subjects enrolled | Romania: 892             |
| Country: Number of subjects enrolled | Russian Federation: 2119 |
| Country: Number of subjects enrolled | Serbia: 210              |
| Country: Number of subjects enrolled | Singapore: 21            |
| Country: Number of subjects enrolled | Slovenia: 68             |
| Country: Number of subjects enrolled | South Africa: 374        |
| Country: Number of subjects enrolled | Spain: 235               |
| Country: Number of subjects enrolled | Sweden: 57               |
| Country: Number of subjects enrolled | Switzerland: 50          |
| Country: Number of subjects enrolled | Taiwan: 198              |
| Country: Number of subjects enrolled | Thailand: 96             |
| Country: Number of subjects enrolled | Turkey: 96               |
| Country: Number of subjects enrolled | Ukraine: 1894            |
| Country: Number of subjects enrolled | United Kingdom: 118      |
| Country: Number of subjects enrolled | Uruguay: 29              |
| Country: Number of subjects enrolled | Vietnam: 171             |
| Country: Number of subjects enrolled | Argentina: 954           |
| Country: Number of subjects enrolled | Armenia: 239             |
| Country: Number of subjects enrolled | Australia: 116           |
| Country: Number of subjects enrolled | Austria: 19              |
| Country: Number of subjects enrolled | Belgium: 52              |
| Country: Number of subjects enrolled | Brazil: 853              |
| Country: Number of subjects enrolled | Bulgaria: 1121           |
| Country: Number of subjects enrolled | Canada: 254              |
| Country: Number of subjects enrolled | China: 975               |
| Country: Number of subjects enrolled | Croatia: 197             |
| Country: Number of subjects enrolled | Czech Republic: 539      |
| Country: Number of subjects enrolled | Denmark: 76              |
| Country: Number of subjects enrolled | Estonia: 387             |
| Country: Number of subjects enrolled | Finland: 8               |
| Country: Number of subjects enrolled | France: 99               |
| Country: Number of subjects enrolled | Georgia: 102             |
| Country: Number of subjects enrolled | Germany: 309             |
| Country: Number of subjects enrolled | Greece: 77               |
| Country: Number of subjects enrolled | Hungary: 981             |
| Country: Number of subjects enrolled | Slovakia: 379            |
| Country: Number of subjects enrolled | India: 295               |
| Country: Number of subjects enrolled | Ireland: 47              |
| Country: Number of subjects enrolled | Italy: 384               |
| Worldwide total number of subjects   | 19102                    |
| EEA total number of subjects         | 8582                     |

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          | 0 |

|                           |       |
|---------------------------|-------|
| months)                   |       |
| Children (2-11 years)     | 0     |
| Adolescents (12-17 years) | 0     |
| Adults (18-64 years)      | 10205 |
| From 65 to 84 years       | 8789  |
| 85 years and over         | 108   |

## Subject disposition

### Recruitment

Recruitment details:

A total of 1181 centres in 51 countries screened at least one patient and 1139 centres included at least one patient.

### Pre-assignment

Screening details:

A total of 23 164 patients were screened, 21 862 were selected and 19 107 were included. The Randomised Set comprised 19 102 patients: 9550 patients in the ivabradine group and 9552 in the placebo group. Of the 19 102 patients in the Randomised Set, 17 724 completed the study: 8830 patients in the ivabradine group and 8894 in the placebo group.

### Period 1

|                              |                                            |
|------------------------------|--------------------------------------------|
| Period 1 title               | Post-randomisation period (overall period) |
| Is this the baseline period? | Yes                                        |
| Allocation method            | Randomised - controlled                    |
| Blinding used                | Double blind                               |
| Roles blinded                | Subject, Investigator                      |

### Arms

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

Arm description:

Patients taking Ivabradine

|                                        |            |
|----------------------------------------|------------|
| Arm type                               | Study drug |
| Investigational medicinal product name | Ivabradine |
| Investigational medicinal product code |            |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

5 mg, 7.5 mg or 10 mg tablets to be taken orally twice daily at 12-hours intervals, in the morning and in the evening during meals.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Patients taking placebo

|                                        |          |
|----------------------------------------|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

5 mg, 7.5 mg or 10 mg matching tablets to be taken orally twice daily at 12-hours intervals, in the morning and in the evening during meals.

| <b>Number of subjects in period 1</b> | Ivabradine | Placebo |
|---------------------------------------|------------|---------|
| Started                               | 9550       | 9552    |
| Completed                             | 8830       | 8894    |
| Not completed                         | 720        | 658     |
| Adverse event, serious fatal          | 485        | 458     |
| Physician decision                    | 1          | -       |
| Consent withdrawn by subject          | 231        | 199     |
| Lost to follow-up                     | 3          | 1       |

## Baseline characteristics

### Reporting groups

|                                                            |            |
|------------------------------------------------------------|------------|
| Reporting group title                                      | Ivabradine |
| Reporting group description:<br>Patients taking Ivabradine |            |
| Reporting group title                                      | Placebo    |
| Reporting group description:<br>Patients taking placebo    |            |

| Reporting group values                                | Ivabradine | Placebo | Total |
|-------------------------------------------------------|------------|---------|-------|
| Number of subjects                                    | 9550       | 9552    | 19102 |
| Age categorical<br>Units: Subjects                    |            |         |       |
| In utero                                              | 0          | 0       | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0          | 0       | 0     |
| Newborns (0-27 days)                                  | 0          | 0       | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0          | 0       | 0     |
| Children (2-11 years)                                 | 0          | 0       | 0     |
| Adolescents (12-17 years)                             | 0          | 0       | 0     |
| Adults (18-64 years)                                  | 5109       | 5096    | 10205 |
| From 65-84 years                                      | 4387       | 4402    | 8789  |
| 85 years and over                                     | 54         | 54      | 108   |
| Age continuous<br>Units: years                        |            |         |       |
| arithmetic mean                                       | 65         | 65      |       |
| standard deviation                                    | ± 7.2      | ± 7.3   | -     |
| Gender categorical<br>Units: Subjects                 |            |         |       |
| Female                                                | 2601       | 2662    | 5263  |
| Male                                                  | 6949       | 6890    | 13839 |

### Subject analysis sets

|                                                                                                                                                                            |                       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Subject analysis set title                                                                                                                                                 | Randomised set        |
| Subject analysis set type                                                                                                                                                  | Intention-to-treat    |
| Subject analysis set description:<br>All included patients with a randomisation number allocated by the IRS.                                                               |                       |
| Subject analysis set title                                                                                                                                                 | Safety set            |
| Subject analysis set type                                                                                                                                                  | Safety analysis       |
| Subject analysis set description:<br>All patients having received at least one dose of study drug.                                                                         |                       |
| Subject analysis set title                                                                                                                                                 | Randomised set angina |
| Subject analysis set type                                                                                                                                                  | Intention-to-treat    |
| Subject analysis set description:<br>All symptomatic angina patients of the RS having a CCS class ≥ II at baseline (defined as CCS class ≥ II at selection and inclusion). |                       |
| Subject analysis set title                                                                                                                                                 | Safety set angina     |

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

All symptomatic angina patients of the SS having a CCS class  $\geq$  II at baseline (defined as CCS class  $\geq$  II at selection and inclusion).

| Reporting group values                             | Randomised set | Safety set | Randomised set angina |
|----------------------------------------------------|----------------|------------|-----------------------|
| Number of subjects                                 | 19102          | 19083      | 1204                  |
| Age categorical<br>Units: Subjects                 |                |            |                       |
| In utero                                           | 0              |            |                       |
| Preterm newborn infants (gestational age < 37 wks) | 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)                               | 5109           |            |                       |
| From 65-84 years                                   | 4387           |            |                       |
| 85 years and over                                  | 54             |            |                       |
| Age continuous<br>Units: years                     |                |            |                       |
| arithmetic mean                                    | 65             |            |                       |
| standard deviation                                 | $\pm 7.2$      | $\pm$      | $\pm$                 |
| Gender categorical<br>Units: Subjects              |                |            |                       |
| Female                                             | 5263           |            |                       |
| Male                                               | 13839          |            |                       |

| Reporting group values                             | Safety set angina |  |  |
|----------------------------------------------------|-------------------|--|--|
| Number of subjects                                 | 1203              |  |  |
| Age categorical<br>Units: Subjects                 |                   |  |  |
| In utero                                           |                   |  |  |
| Preterm newborn infants (gestational age < 37 wks) |                   |  |  |
| Newborns (0-27 days)                               |                   |  |  |
| Infants and toddlers (28 days-23 months)           |                   |  |  |
| Children (2-11 years)                              |                   |  |  |
| Adolescents (12-17 years)                          |                   |  |  |
| Adults (18-64 years)                               |                   |  |  |
| From 65-84 years                                   |                   |  |  |
| 85 years and over                                  |                   |  |  |
| Age continuous<br>Units: years                     |                   |  |  |
| arithmetic mean                                    |                   |  |  |
| standard deviation                                 | $\pm$             |  |  |
| Gender categorical<br>Units: Subjects              |                   |  |  |
| Female                                             |                   |  |  |
| Male                                               |                   |  |  |





## End points

### End points reporting groups

|                                                                                                                                                 |                       |
|-------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Reporting group title                                                                                                                           | Ivabradine            |
| Reporting group description:                                                                                                                    |                       |
| Patients taking Ivabradine                                                                                                                      |                       |
| Reporting group title                                                                                                                           | Placebo               |
| Reporting group description:                                                                                                                    |                       |
| Patients taking placebo                                                                                                                         |                       |
| Subject analysis set title                                                                                                                      | Randomised set        |
| Subject analysis set type                                                                                                                       | Intention-to-treat    |
| Subject analysis set description:                                                                                                               |                       |
| All included patients with a randomisation number allocated by the IRS.                                                                         |                       |
| Subject analysis set title                                                                                                                      | Safety set            |
| Subject analysis set type                                                                                                                       | Safety analysis       |
| Subject analysis set description:                                                                                                               |                       |
| All patients having received at least one dose of study drug.                                                                                   |                       |
| Subject analysis set title                                                                                                                      | Randomised set angina |
| Subject analysis set type                                                                                                                       | Intention-to-treat    |
| Subject analysis set description:                                                                                                               |                       |
| All symptomatic angina patients of the RS having a CCS class $\geq$ II at baseline (defined as CCS class $\geq$ II at selection and inclusion). |                       |
| Subject analysis set title                                                                                                                      | Safety set angina     |
| Subject analysis set type                                                                                                                       | Safety analysis       |
| Subject analysis set description:                                                                                                               |                       |
| All symptomatic angina patients of the SS having a CCS class $\geq$ II at baseline (defined as CCS class $\geq$ II at selection and inclusion). |                       |

### Primary: Primary composite endpoint

|                                                                                                                                                                  |                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| End point title                                                                                                                                                  | Primary composite endpoint |
| End point description:                                                                                                                                           |                            |
| First event among cardiovascular death or non-fatal MI                                                                                                           |                            |
| End point type                                                                                                                                                   | Primary                    |
| End point timeframe:                                                                                                                                             |                            |
| All criteria are expressed as the time to first event, defined as the duration between the date of randomisation and the date of first occurrence of this event. |                            |

| End point values            | Ivabradine      | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 9550            | 9552            |  |  |
| Units: number of events     | 654             | 611             |  |  |

## Statistical analyses

|                                         |                                          |
|-----------------------------------------|------------------------------------------|
| <b>Statistical analysis title</b>       | Superiority of Ivabradine versus Placebo |
| Comparison groups                       | Ivabradine v Placebo                     |
| Number of subjects included in analysis | 19102                                    |
| Analysis specification                  | Pre-specified                            |
| Analysis type                           | superiority                              |
| P-value                                 | = 0.1969                                 |
| Method                                  | Regression, Cox                          |
| Parameter estimate                      | Cox proportional hazard                  |
| Point estimate                          | 1.08                                     |
| Confidence interval                     |                                          |
| level                                   | 95 %                                     |
| sides                                   | 2-sided                                  |
| lower limit                             | 0.96                                     |
| upper limit                             | 1.2                                      |
| Variability estimate                    | Standard error of the mean               |
| Dispersion value                        | 0.06                                     |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

On treatment

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

### Reporting groups

|                       |            |
|-----------------------|------------|
| Reporting group title | Ivabradine |
|-----------------------|------------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events                                              | Ivabradine              | Placebo                 |  |
|---------------------------------------------------------------------|-------------------------|-------------------------|--|
| Total subjects affected by serious adverse events                   |                         |                         |  |
| subjects affected / exposed                                         | 3379 / 9539<br>(35.42%) | 3263 / 9544<br>(34.19%) |  |
| number of deaths (all causes)                                       | 363                     | 356                     |  |
| number of deaths resulting from adverse events                      | 1                       | 0                       |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                         |                         |  |
| Acute leukaemia                                                     |                         |                         |  |
| subjects affected / exposed                                         | 1 / 9539 (0.01%)        | 0 / 9544 (0.00%)        |  |
| occurrences causally related to treatment / all                     | 0 / 1                   | 0 / 0                   |  |
| deaths causally related to treatment / all                          | 0 / 1                   | 0 / 0                   |  |
| Acute myeloid leukaemia                                             |                         |                         |  |
| subjects affected / exposed                                         | 0 / 9539 (0.00%)        | 1 / 9544 (0.01%)        |  |
| occurrences causally related to treatment / all                     | 0 / 0                   | 0 / 1                   |  |
| deaths causally related to treatment / all                          | 0 / 0                   | 0 / 0                   |  |
| Adenocarcinoma gastric                                              |                         |                         |  |
| subjects affected / exposed                                         | 6 / 9539 (0.06%)        | 4 / 9544 (0.04%)        |  |
| occurrences causally related to treatment / all                     | 0 / 6                   | 0 / 4                   |  |
| deaths causally related to treatment / all                          | 0 / 1                   | 0 / 2                   |  |
| Adenocarcinoma of colon                                             |                         |                         |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adenocarcinoma pancreas                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adenolymphoma                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adenosquamous cell lung cancer                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Anal squamous cell carcinoma                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Angiofibroma                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Astrocytoma, low grade                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| B precursor type acute leukaemia                |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| B-cell lymphoma                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Basal cell carcinoma                            |                   |                   |  |
| subjects affected / exposed                     | 24 / 9539 (0.25%) | 21 / 9544 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 25            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Basosquamous carcinoma                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Basosquamous carcinoma of skin                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign breast neoplasm                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign neoplasm of prostate                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign neoplasm of thyroid gland                |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign pleural neoplasm                         |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign renal neoplasm                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder cancer recurrent                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder cancer stage I, with cancer in situ     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder cancer stage II                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder neoplasm                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder papilloma                               |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder transitional cell carcinoma             |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder transitional cell carcinoma recurrent   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder transitional cell carcinoma stage II    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder transitional cell carcinoma stage III   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bowen's disease                                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain cancer metastatic                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Brain neoplasm malignant                        |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Brain stem glioma                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Breast cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Breast cancer recurrent                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast cancer stage I                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast cancer stage II                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchial carcinoma                             |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchioloalveolar carcinoma                    |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cancer pain                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carcinoid tumour of the stomach                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid body tumour                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Castleman's disease                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral hygroma                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervix carcinoma                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cervix carcinoma stage III                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholangiocarcinoma                              |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cholesteatoma                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic lymphocytic leukaemia                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic lymphocytic leukaemia stage 2           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clear cell renal cell carcinoma                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clear cell sarcoma of soft tissue               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon adenoma                                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon cancer                                    |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon cancer metastatic                         |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 1            |  |
| Colon cancer stage 0                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colorectal cancer metastatic                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diffuse large B-cell lymphoma                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diffuse large B-cell lymphoma stage III         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diffuse large B-cell lymphoma stage IV          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ear neoplasm malignant                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endometrial adenocarcinoma                      |                  |                  |  |

|                                                      |                  |                  |  |
|------------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                          | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Ependymoma                                           |                  |                  |  |
| subjects affected / exposed                          | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Extranodal marginal zone B-cell lymphoma (MALT type) |                  |                  |  |
| subjects affected / exposed                          | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Gallbladder cancer                                   |                  |                  |  |
| subjects affected / exposed                          | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Gallbladder neoplasm                                 |                  |                  |  |
| subjects affected / exposed                          | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Gastric adenoma                                      |                  |                  |  |
| subjects affected / exposed                          | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Gastric cancer                                       |                  |                  |  |
| subjects affected / exposed                          | 3 / 9539 (0.03%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all      | 0 / 3            | 0 / 8            |  |
| deaths causally related to treatment / all           | 0 / 1            | 0 / 2            |  |
| Gastric cancer stage IV                              |                  |                  |  |
| subjects affected / exposed                          | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Gastrointestinal carcinoma                           |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal stromal tumour                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal tract adenoma                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrooesophageal cancer                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glioblastoma                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Haemangioma of bone                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 0            |  |
| Hepatic cancer metastatic                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 2            |  |
| Hepatocellular carcinoma                        |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hodgkin's disease                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal adenocarcinoma                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large cell lung cancer                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large cell lung cancer metastatic               |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Large cell lung cancer stage II                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large intestine benign neoplasm                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngeal cancer                                |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngeal cancer metastatic                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Laryngeal cancer recurrent                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Laryngeal squamous cell carcinoma               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Lentigo maligna                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lip and/or oral cavity cancer                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Lip and/or oral cavity cancer stage IV          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lipoma                                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung adenocarcinoma                             |                  |                  |  |



|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lung adenocarcinoma metastatic                  |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 6             |  |
| Lung adenocarcinoma stage IV                    |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lung cancer metastatic                          |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 6             |  |
| Lung carcinoma cell type unspecified stage II   |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| 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 IV   |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Lung neoplasm                                   |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2             |  |
| Lung neoplasm malignant                         |                  |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 5             |  |
| Lung squamous cell carcinoma metastatic         |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Lung squamous cell carcinoma stage III          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphangiosis carcinomatosa                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Malignant ascites                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant glioma                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Malignant melanoma                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant neoplasm of ampulla of Vater          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant neoplasm of choroid                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant neoplasm of eyelid                    |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant oligodendroglioma                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Malignant pleural effusion                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meningioma                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesothelioma                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to abdominal cavity                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to adrenals                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to bone                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Metastases to bone marrow                       |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to central nervous system            |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Metastases to eye                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to liver                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Metastases to lung                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to lymph nodes                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastases to peritoneum                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastases to the mediastinum                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to spine                             |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastatic bronchial carcinoma                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Metastatic carcinoma of the bladder             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastatic gastric cancer                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 2            |  |
| Metastatic malignant melanoma                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastatic neoplasm                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastatic renal cell carcinoma                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Metastatic pain                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastatic squamous cell carcinoma              |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastatic uterine cancer                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Myelodysplastic syndrome                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myelofibrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myeloproliferative disorder                     |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasopharyngeal cancer                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Neoplasm                                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neoplasm skin                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuroendocrine carcinoma metastatic             |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuroendocrine tumour                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuroma                                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nodular melanoma                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-Hodgkin's lymphoma                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Non-small cell lung cancer                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Non-small cell lung cancer metastatic           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-small cell lung cancer stage IIIA           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal adenocarcinoma                      |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal adenocarcinoma metastatic           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal carcinoma                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Oesophageal squamous cell carcinoma             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Oropharyngeal cancer                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian adenoma                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Ovarian cancer metastatic                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian epithelial cancer metastatic            |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian germ cell teratoma benign               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatic carcinoma                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pancreatic carcinoma metastatic                 |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 4            | 0 / 3            |  |
| Pancreatic neoplasm                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Papillary tumour of renal pelvis                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parathyroid tumour benign                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Penis carcinoma stage II                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pharyngeal cancer recurrent                     |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Pineal parenchymal neoplasm malignant           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Pituitary tumour benign                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pituitary tumour recurrent                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Plasma cell leukaemia                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Plasma cell myeloma                             |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 2            |  |
| Pleural mesothelioma                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleural neoplasm                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polycythaemia vera                              |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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                     | 38 / 9539 (0.40%) | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 38            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer metastatic                      |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Prostate cancer recurrent                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer stage I                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer stage II                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer stage III                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostate cancer stage IV                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Prostatic adenoma                               |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal adenocarcinoma                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Rectal cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Rectal cancer recurrent                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal cancer stage 0                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal cancer stage IV                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Rectosigmoid cancer                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal neoplasm                                 |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 6 / 9539 (0.06%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Renal cancer metastatic                         |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cancer stage I                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal oncocytoma                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cell carcinoma                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rhabdomyosarcoma                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland adenoma                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland cancer                           |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin cancer metastatic                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small cell lung cancer                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Small cell lung cancer metastatic               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Small intestine carcinoma                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal meningioma benign                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Squamous cell carcinoma                         |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Squamous cell carcinoma of head and neck        |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma of lung                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 2            |  |
| Squamous cell carcinoma of pharynx              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma of skin                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma of the cervix           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Squamous cell carcinoma of the hypopharynx      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma of the oral cavity      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Testicular cancer metastatic                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Throat cancer                                   |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroid cancer metastatic                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tongue neoplasm malignant stage unspecified     |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Tonsil cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Transitional cell carcinoma                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urethral cancer metastatic                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Uterine leiomyoma                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vulval cancer                                   |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular disorders                              |                  |                  |  |
| Aortic aneurysm                                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic aneurysm rupture                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Aortic arteriosclerosis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic dilatation                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic dissection                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic occlusion                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic thrombosis                               |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial rupture                                |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arterial stenosis                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriosclerosis                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood pressure fluctuation                      |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood pressure inadequately controlled          |                   |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 1 / 8             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Circulatory collapse                            |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Deep vein thrombosis                            |                   |                   |  |
| subjects affected / exposed                     | 19 / 9539 (0.20%) | 17 / 9544 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 19            | 1 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Diabetic macroangiopathy                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic microangiopathy                        |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic vascular disorder                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Embolism                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Essential hypertension                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 5 / 9539 (0.05%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Femoral artery aneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Femoral artery dissection                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Femoral artery occlusion                        |                  |                  |  |

|                                                 |                    |                    |  |
|-------------------------------------------------|--------------------|--------------------|--|
| subjects affected / exposed                     | 10 / 9539 (0.10%)  | 14 / 9544 (0.15%)  |  |
| occurrences causally related to treatment / all | 0 / 11             | 0 / 15             |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Haemorrhage                                     |                    |                    |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)   | 1 / 9544 (0.01%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Hypertension                                    |                    |                    |  |
| subjects affected / exposed                     | 204 / 9539 (2.14%) | 144 / 9544 (1.51%) |  |
| occurrences causally related to treatment / all | 2 / 220            | 0 / 152            |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Hypertensive crisis                             |                    |                    |  |
| subjects affected / exposed                     | 104 / 9539 (1.09%) | 105 / 9544 (1.10%) |  |
| occurrences causally related to treatment / all | 1 / 117            | 0 / 119            |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Hypertensive emergency                          |                    |                    |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%)  | 8 / 9544 (0.08%)   |  |
| occurrences causally related to treatment / all | 1 / 15             | 0 / 8              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Hypotension                                     |                    |                    |  |
| subjects affected / exposed                     | 25 / 9539 (0.26%)  | 36 / 9544 (0.38%)  |  |
| occurrences causally related to treatment / all | 5 / 26             | 0 / 37             |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Hypovolaemic shock                              |                    |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 4 / 9544 (0.04%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 4              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 1              |  |
| Iliac artery occlusion                          |                    |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 4 / 9544 (0.04%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 4              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Iliac artery rupture                            |                    |                    |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intermittent claudication                       |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Jugular vein thrombosis                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Labile blood pressure                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Labile hypertension                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leriche syndrome                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphoedema                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphostasis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant hypertension                          |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Orthostatic hypotension                         |                   |                   |  |
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 2 / 12            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pallor                                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral arterial occlusive disease           |                   |                   |  |
| subjects affected / exposed                     | 52 / 9539 (0.55%) | 67 / 9544 (0.70%) |  |
| occurrences causally related to treatment / all | 0 / 58            | 0 / 70            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery aneurysm                      |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery dissection                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery stenosis                      |                   |                   |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery thrombosis                    |                   |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral embolism                             |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral ischaemia                            |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Peripheral vascular disorder                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Phlebitis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Phlebitis superficial                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shock haemorrhagic                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Subclavian artery occlusion                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subclavian artery stenosis                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subclavian steal syndrome                       |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subgaleal haematoma                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Systolic hypertension                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombophlebitis                                |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombophlebitis superficial                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombosis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Varicose vein                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vasculitis                                      |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vasculitis necrotising                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vena cava thrombosis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous insufficiency                            |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous thrombosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous thrombosis limb                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Withdrawal hypertension                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Surgical and medical procedures                 |                  |                  |  |
| Abdominal hernia repair                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Alcohol detoxification                          |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic aneurysm repair                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic bypass                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic valve repair                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic valve replacement                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial bypass operation                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial stent insertion                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous fistula operation                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder neoplasm surgery                        |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blepharoplasty                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bunion operation                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac ablation                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac aneurysm repair                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac rehabilitation therapy                  |                   |                   |  |
| subjects affected / exposed                     | 23 / 9539 (0.24%) | 19 / 9544 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 30            | 0 / 27            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carotid angioplasty                             |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carotid artery bypass                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carotid artery stent insertion                  |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid endarterectomy                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cataract operation                              |                  |                  |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chemotherapy                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholecystectomy                                 |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholesteatoma removal                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Circumcision                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary angioplasty                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary arterial stent insertion               |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary artery bypass                          |                   |                   |  |
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary revascularisation                      |                   |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetes mellitus management                    |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Dupuytren's contracture operation               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Fasciectomy                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Femoral hernia repair                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Finger amputation                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrectomy                                     |                   |                   |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Gastric banding                                 |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Gastric bypass                                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Glaucoma surgery                                |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hip arthroplasty                                |                  |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 9 / 9544 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 10           | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hospitalisation                                 |                  |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 13           | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hydrocele operation                             |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Ileostomy closure                               |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Implantable defibrillator insertion             |                  |                   |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Incisional hernia repair                        |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Infusion                                        |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Inguinal hernia repair                          |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 9 / 9544 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Internal fixation of fracture                   |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Intraocular lens extraction                     |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Keratoplasty                                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Knee arthroplasty                               |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Knee operation                                  |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leg amputation                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lens extraction                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Medical device removal                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver operation                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meniscus removal                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metatarsal excision                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mitral valve repair                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal polypectomy                               |                  |                  |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Obesity surgery                                 |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Nasal septal operation                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Oophorectomy bilateral                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Percutaneous coronary intervention              |                   |                   |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 16 / 9544 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Peripheral artery angioplasty                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery bypass                        |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral artery stent insertion               |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Physiotherapy                                   |                   |                   |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Radical hysterectomy                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Radiotherapy                                    |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Rehabilitation therapy                          |                  |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 12           | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Removal of internal fixation                    |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Renal artery ablation                           |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Renal stone removal                             |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Retinal laser coagulation                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Rotator cuff repair                             |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shoulder arthroplasty                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus operation                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin neoplasm excision                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal operation                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Suture insertion                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroidectomy                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toe amputation                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transurethral prostatectomy                     |                  |                  |  |

|                                                      |                  |                  |  |
|------------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                          | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all      | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Umbilical hernia repair                              |                  |                  |  |
| subjects affected / exposed                          | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Urethral dilation procedure                          |                  |                  |  |
| subjects affected / exposed                          | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Urinary calculus removal                             |                  |                  |  |
| subjects affected / exposed                          | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Uterine polypectomy                                  |                  |                  |  |
| subjects affected / exposed                          | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Vaginal prolapse repair                              |                  |                  |  |
| subjects affected / exposed                          | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| General disorders and administration site conditions |                  |                  |  |
| Apparent death                                       |                  |                  |  |
| subjects affected / exposed                          | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Asthenia                                             |                  |                  |  |
| subjects affected / exposed                          | 3 / 9539 (0.03%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all      | 0 / 3            | 2 / 6            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Cardiac death                                        |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |  |
| Chest discomfort                                |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 1 / 3             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chest pain                                      |                   |                   |  |
| subjects affected / exposed                     | 32 / 9539 (0.34%) | 36 / 9544 (0.38%) |  |
| occurrences causally related to treatment / all | 0 / 35            | 0 / 50            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chills                                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Death                                           |                   |                   |  |
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 10            | 0 / 7             |  |
| Device breakage                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device dislocation                              |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device extrusion                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device failure                                  |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device malfunction                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device occlusion                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Discomfort                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Drowning                                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Drug interaction                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Face oedema                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fatigue                                         |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 2 / 7            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Feeling abnormal                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Feeling cold                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Foreign body reaction                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gait disturbance                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| General physical health deterioration           |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Generalised oedema                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hernia obstructive                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Impaired healing                                |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Inflammation                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Irritability                                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Malaise                                         |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Medical device complication                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Multi-organ failure                             |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 3             |  |
| Non-cardiac chest pain                          |                   |                   |  |
| subjects affected / exposed                     | 38 / 9539 (0.40%) | 29 / 9544 (0.30%) |  |
| occurrences causally related to treatment / all | 0 / 43            | 1 / 31            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Oedema peripheral                               |                   |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pacemaker generated arrhythmia                  |                   |                   |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pain                                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Puncture site haemorrhage                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pyrexia                                         |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spinal pain                                     |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Stent-graft endoleak                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sudden cardiac death                            |                   |                   |  |
| subjects affected / exposed                     | 43 / 9539 (0.45%) | 46 / 9544 (0.48%) |  |
| occurrences causally related to treatment / all | 0 / 43            | 0 / 46            |  |
| deaths causally related to treatment / all      | 0 / 43            | 0 / 46            |  |
| Sudden death                                    |                   |                   |  |
| subjects affected / exposed                     | 75 / 9539 (0.79%) | 74 / 9544 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 75            | 0 / 74            |  |
| deaths causally related to treatment / all      | 0 / 75            | 0 / 74            |  |
| Systemic inflammatory response syndrome         |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombosis in device                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Immune system disorders                         |                  |                  |  |
| Allergy to arthropod sting                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Amyloidosis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaphylactic reaction                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaphylactic shock                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Drug hypersensitivity                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Food allergy                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypersensitivity                                |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Social circumstances                            |                   |                   |  |
| Activities of daily living impaired             |                   |                   |  |
| subjects affected / exposed                     | 11 / 9539 (0.12%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 11 / 11           | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Alcohol use                                     |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Immobile                                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Impaired driving ability                        |                   |                   |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 15 / 15           | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Reproductive system and breast disorders        |                   |                   |  |
| Acquired hydrocele                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Acquired phimosis                               |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Benign prostatic hyperplasia                    |                   |                   |  |
| subjects affected / exposed                     | 23 / 9539 (0.24%) | 28 / 9544 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 23            | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| Breast disorder                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystocele                                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epididymitis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Female genital tract fistula                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gynaecomastia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic adhesions                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatitis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatomegaly                                  |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Uterine prolapse                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Uterovaginal prolapse                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vaginal haemorrhage                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Varicocele                                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vulval disorder                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory, thoracic and mediastinal disorders |                   |                   |  |
| Acquired tracheo-oesophageal fistula            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Acute pulmonary oedema                          |                   |                   |  |
| subjects affected / exposed                     | 31 / 9539 (0.32%) | 30 / 9544 (0.31%) |  |
| occurrences causally related to treatment / all | 0 / 33            | 0 / 32            |  |
| deaths causally related to treatment / all      | 0 / 4             | 0 / 4             |  |
| Acute respiratory distress syndrome             |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Acute respiratory failure                       |                   |                   |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 1 / 13            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 1             |  |
| Alveolitis allergic                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Asphyxia                                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Asthma                                          |                   |                   |  |
| subjects affected / exposed                     | 21 / 9539 (0.22%) | 16 / 9544 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 22            | 0 / 21            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Aspiration                                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Asthmatic crisis                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Atelectasis                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchiectasis                                  |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchitis chronic                              |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchopneumopathy                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchospasm                                    |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 1 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Choking                                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chronic obstructive pulmonary disease           |                   |                   |  |
| subjects affected / exposed                     | 64 / 9539 (0.67%) | 52 / 9544 (0.54%) |  |
| occurrences causally related to treatment / all | 0 / 84            | 0 / 62            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Chronic respiratory failure                     |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Cough                                           |                   |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cyanosis central                                |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diaphragmatic paralysis                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Dyspnoea                                        |                   |                   |  |
| subjects affected / exposed                     | 23 / 9539 (0.24%) | 23 / 9544 (0.24%) |  |
| occurrences causally related to treatment / all | 0 / 25            | 2 / 26            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Dyspnoea at rest                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Dyspnoea exertional                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Emphysema                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Epistaxis                                       |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Granulomatous pneumonitis                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haemoptysis                                     |                   |                   |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemothorax                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydropneumothorax                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hydrothorax                                     |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxia                                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Idiopathic pulmonary fibrosis                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Interstitial lung disease                       |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Laryngeal stenosis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung consolidation                              |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung cyst                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung disorder                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung infiltration                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal polyps                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal septum deviation                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Obstructive airways disorder                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pharyngeal oedema                               |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pickwickian syndrome                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleural effusion                                |                  |                  |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleural fibrosis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleural haemorrhage                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pleurisy                                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia aspiration                            |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pneumonitis                                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumothorax                                    |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pulmonary arterial hypertension                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pulmonary artery thrombosis                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pulmonary congestion                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| 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                     | 15 / 9539 (0.16%) | 24 / 9544 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 24            |  |
| deaths causally related to treatment / all      | 0 / 5             | 0 / 8             |  |
| Pulmonary fibrosis                              |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Pulmonary granuloma                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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                     | 19 / 9539 (0.20%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 19            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 0             |  |
| Pulmonary mass                                  |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pulmonary microemboli                           |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Pulmonary oedema                                |                   |                   |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Pulmonary thrombosis                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Reflux laryngitis                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiration abnormal                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory acidosis                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory arrest                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Respiratory disorder                            |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory distress                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory failure                             |                   |                   |  |
| subjects affected / exposed                     | 21 / 9539 (0.22%) | 27 / 9544 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 21            | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 5             | 0 / 6             |  |
| Sinus polyp                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sleep apnoea syndrome                           |                   |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Snoring                                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Status asthmaticus                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tachypnoea                                      |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vocal cord polyp                                |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wheezing                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psychiatric disorders                           |                  |                  |  |
| Acute psychosis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Aggression                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Agitated depression                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Agitation                                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Alcohol abuse                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Alcohol withdrawal syndrome                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Alcoholism                                      |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Anxiety                                         |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Bipolar I disorder                              |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Bipolar disorder                                |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Completed suicide                               |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 4             |  |
| Confusional state                               |                  |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 7            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Delirium                                        |                  |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Delirium tremens                                |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Delusional disorder, unspecified type           |                  |                   |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Depressed mood                                  |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 1 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Depression                                      |                   |                   |  |
| subjects affected / exposed                     | 57 / 9539 (0.60%) | 54 / 9544 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 59            | 0 / 54            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Depression suicidal                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Depressive symptom                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Disorientation                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Dysthymic disorder                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hallucination                                   |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hallucination, auditory                         |                   |                   |  |

|                                                  |                  |                  |  |
|--------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                      | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all  | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Hallucination, visual                            |                  |                  |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Hallucinations, mixed                            |                  |                  |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Impulsive behaviour                              |                  |                  |  |
| subjects affected / exposed                      | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all  | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Insomnia                                         |                  |                  |  |
| subjects affected / exposed                      | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all  | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Intentional drug misuse                          |                  |                  |  |
| subjects affected / exposed                      | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all  | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Major depression                                 |                  |                  |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Mood disorder due to a general medical condition |                  |                  |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Nervousness                                      |                  |                  |  |

|                                                       |                  |                  |  |
|-------------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                           | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Obsessive thoughts                                    |                  |                  |  |
| subjects affected / exposed                           | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Panic attack                                          |                  |                  |  |
| subjects affected / exposed                           | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Paranoia                                              |                  |                  |  |
| subjects affected / exposed                           | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Persecutory delusion                                  |                  |                  |  |
| subjects affected / exposed                           | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Psychomotor retardation                               |                  |                  |  |
| subjects affected / exposed                           | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Psychosomatic disease                                 |                  |                  |  |
| subjects affected / exposed                           | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all       | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Psychotic disorder due to a general medical condition |                  |                  |  |
| subjects affected / exposed                           | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Psychotic disorder                                    |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Sleep disorder                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sleep terror                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stress                                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Suicidal ideation                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Suicide attempt                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatobiliary disorders                         |                  |                  |  |
| Acute hepatic failure                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Alcoholic liver disease                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bile duct stone                                 |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Biliary cirrhosis primary                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Biliary colic                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Biliary tract disorder                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholangitis                                     |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholecystitis                                   |                   |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%)  | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholangitis acute                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholecystitis acute                             |                   |                   |  |
| subjects affected / exposed                     | 19 / 9539 (0.20%) | 17 / 9544 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 19            | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholecystitis chronic                           |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 9539 (0.07%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholelithiasis                                  |                   |                   |  |
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 20 / 9544 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Cholestasis                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chronic hepatitis                               |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cirrhosis alcoholic                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Drug-induced liver injury                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gallbladder perforation                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gallbladder polyp                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hepatic cirrhosis                               |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hepatic congestion                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cyst                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic failure                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hepatic mass                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic steatosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis acute                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis alcoholic                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis cholestatic                           |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatomegaly                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperbilirubinaemia                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic hepatitis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Jaundice                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Jaundice cholestatic                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver disorder                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver injury                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Portal vein thrombosis                          |                  |                  |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sphincter of Oddi dysfunction                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Post cholecystectomy syndrome                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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                     | 11 / 9539 (0.12%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 1 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Amylase increased                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriogram carotid                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriogram coronary                            |                   |                   |  |
| subjects affected / exposed                     | 43 / 9539 (0.45%) | 53 / 9544 (0.56%) |  |
| occurrences causally related to treatment / all | 0 / 45            | 0 / 58            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arthroscopy                                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Aspartate aminotransferase increased            |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 1 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Biopsy prostate                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood alkaline phosphatase increased            |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood creatine phosphokinase increased          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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                     | 3 / 9539 (0.03%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood glucose decreased                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood glucose increased                         |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood iron decreased                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood lactate dehydrogenase increased           |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood parathyroid hormone decreased             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood potassium decreased                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood potassium increased                       |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood pressure decreased                        |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood pressure increased                        |                   |                   |  |
| subjects affected / exposed                     | 24 / 9539 (0.25%) | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood pressure systolic decreased               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood pressure systolic increased               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood triglycerides increased                   |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Body temperature increased                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| C-reactive protein increased                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac enzymes increased                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carbohydrate antigen 19-9 increased             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac stress test abnormal                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiovascular evaluation                       |                   |                   |  |
| subjects affected / exposed                     | 78 / 9539 (0.82%) | 84 / 9544 (0.88%) |  |
| occurrences causally related to treatment / all | 0 / 98            | 0 / 100           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Catheterisation cardiac                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cystoscopy normal                               |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chest X-ray abnormal                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| ECG signs of myocardial ischaemia               |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ejection fraction decreased                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Electrocardiogram QT prolonged                  |                   |                   |  |
| subjects affected / exposed                     | 57 / 9539 (0.60%) | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all | 42 / 60           | 6 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Electrocardiogram ST segment depression         |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Electrocardiogram ST segment elevation          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Electrocardiogram T wave inversion              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Electrocardiogram ambulatory                    |                   |                   |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Electrocardiogram change                        |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Electrocardiogram repolarisation abnormality    |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Fibrin D dimer increased                        |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gamma-glutamyltransferase increased             |                   |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Gastrointestinal examination                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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                     | 2 / 9539 (0.02%)  | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Heart rate decreased                            |                   |                  |  |
| subjects affected / exposed                     | 55 / 9539 (0.58%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 40 / 55           | 4 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hepatic enzyme increased                        |                   |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| International normalised ratio increased        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intraocular pressure increased                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Investigation                                   |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oxygen saturation decreased                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Platelet count decreased                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary arterial pressure increased           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Red blood cell sedimentation rate increased     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Romberg test positive                           |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Sleep study                                     |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Streptococcus test positive                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Stress echocardiogram abnormal                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Thyroid function test abnormal                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Treponema test positive                         |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Troponin increased                              |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Weight decreased                                |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| White blood cell count increased                |                  |                   |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injury, poisoning and procedural complications  |                  |                  |  |
| Abdominal injury                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal wound dehiscence                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Accident                                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Accident at home                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Accidental overdose                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Agitation postoperative                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Alcohol poisoning                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaemia postoperative                           |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ankle fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic injury                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial restenosis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthropod sting                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Back injury                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Blindness traumatic                             |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone fissure                                    |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain contusion                                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Burns second degree                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carbon monoxide poisoning                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cardiac contusion                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac procedure complication                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac valve replacement complication          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac valve rupture                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid artery restenosis                       |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| 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                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Chest injury                                    |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Clavicle fracture                               |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Concussion                                      |                  |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Contusion                                       |                  |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Coronary artery restenosis                      |                  |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Corrosive gastritis                             |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 2 / 9539 (0.02%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Crushing injury of trunk                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Extradural haematoma                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eye contusion                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eye injury                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Face injury                                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Facial bones fracture                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Febrile nonhaemolytic transfusion reaction      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fall                                            |                  |                  |  |

|                                                 |                   |                    |  |
|-------------------------------------------------|-------------------|--------------------|--|
| subjects affected / exposed                     | 95 / 9539 (1.00%) | 109 / 9544 (1.14%) |  |
| occurrences causally related to treatment / all | 4 / 96            | 2 / 109            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Femoral neck fracture                           |                   |                    |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%) | 12 / 9544 (0.13%)  |  |
| occurrences causally related to treatment / all | 0 / 13            | 0 / 12             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Femur fracture                                  |                   |                    |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 10 / 9544 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 10             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Fibula fracture                                 |                   |                    |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 2 / 9544 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 2              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Foot fracture                                   |                   |                    |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)   |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 3              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Foreign body                                    |                   |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Forearm fracture                                |                   |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Foreign body in eye                             |                   |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Hand fracture                                   |                   |                    |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Head injury                                     |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 4            | 2 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Heat stroke                                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hip fracture                                    |                  |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Humerus fracture                                |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Ilium fracture                                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Incisional hernia                               |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Intentional overdose                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Injury                                          |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral disc injury                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal anastomosis complication             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Jaw fracture                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint dislocation                               |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint dislocation postoperative                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint injury                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Kidney rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laceration                                      |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ligament rupture                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ligament sprain                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Limb crushing injury                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Limb injury                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Limb traumatic amputation                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lip injury                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar vertebral fracture                       |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Meniscus injury                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Multiple fractures                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Multiple injuries                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |
| Muscle rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neck injury                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteoradionecrosis                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatic injury                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic fracture                                 |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Penetrating abdominal trauma                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periorbital haematoma                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumoconiosis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumothorax traumatic                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural contusion                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural complication                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Post procedural fistula                         |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Post procedural haematoma                       |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Post procedural haematuria                      |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Post procedural hypothyroidism                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| 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 / 9539 (0.03%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Post procedural myocardial infarction           |                   |                   |  |
| subjects affected / exposed                     | 14 / 9539 (0.15%) | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Post procedural pulmonary embolism              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Post-thoracotomy pain syndrome                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Post-traumatic pain                             |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative thoracic procedure complication   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative ileus                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative wound complication                |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural hypertension                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural hypotension                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural pain                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural site reaction                        |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Radiation oesophagitis                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Radius fracture                                 |                   |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%)  | 15 / 9544 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal haematoma                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Road traffic accident                           |                   |                   |  |
| subjects affected / exposed                     | 23 / 9539 (0.24%) | 26 / 9544 (0.27%) |  |
| occurrences causally related to treatment / all | 0 / 23            | 0 / 26            |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 1             |  |
| Rib fracture                                    |                   |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%)  | 15 / 9544 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Seroma                                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Shunt thrombosis                                |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Silicosis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skull fractured base                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal column injury                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal compression fracture                     |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenic rupture                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stab wound                                      |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Sternal fracture</b>                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Subcutaneous haematoma</b>                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Subdural haematoma</b>                       |                  |                  |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Subdural haemorrhage</b>                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| <b>Suture related complication</b>              |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Tendon injury</b>                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Tendon rupture</b>                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Thoracic vertebral fracture</b>              |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tibia fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tongue injury                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxicity to various agents                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transfusion reaction                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic intracranial haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Traumatic ulcer                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ulna fracture                                   |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper limb fracture                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft complication                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft occlusion                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft thrombosis                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vasoplegia syndrome                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular pseudoaneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound complication                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound necrosis                                  |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wrist fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congenital, familial and genetic disorders      |                  |                  |  |
| Adenomatous polyposis coli                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congenital umbilical hernia                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Factor V Leiden mutation                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolic myopathy                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyloric stenosis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac disorders                               |                  |                  |  |
| Accelerated idioventricular rhythm              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|                                                 |                    |                    |  |
|-------------------------------------------------|--------------------|--------------------|--|
| Acute coronary syndrome                         |                    |                    |  |
| subjects affected / exposed                     | 17 / 9539 (0.18%)  | 21 / 9544 (0.22%)  |  |
| occurrences causally related to treatment / all | 1 / 18             | 0 / 24             |  |
| deaths causally related to treatment / all      | 0 / 4              | 0 / 1              |  |
| Acute left ventricular failure                  |                    |                    |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)   | 5 / 9544 (0.05%)   |  |
| occurrences causally related to treatment / all | 0 / 3              | 0 / 5              |  |
| deaths causally related to treatment / all      | 0 / 1              | 0 / 1              |  |
| Acute myocardial infarction                     |                    |                    |  |
| subjects affected / exposed                     | 200 / 9539 (2.10%) | 208 / 9544 (2.18%) |  |
| occurrences causally related to treatment / all | 2 / 216            | 0 / 229            |  |
| deaths causally related to treatment / all      | 0 / 23             | 0 / 23             |  |
| Adams-Stokes syndrome                           |                    |                    |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)   | 3 / 9544 (0.03%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 1 / 3              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Angina pectoris                                 |                    |                    |  |
| subjects affected / exposed                     | 294 / 9539 (3.08%) | 330 / 9544 (3.46%) |  |
| occurrences causally related to treatment / all | 3 / 314            | 2 / 361            |  |
| deaths causally related to treatment / all      | 0 / 1              | 0 / 0              |  |
| Angina unstable                                 |                    |                    |  |
| subjects affected / exposed                     | 409 / 9539 (4.29%) | 433 / 9544 (4.54%) |  |
| occurrences causally related to treatment / all | 4 / 479            | 0 / 524            |  |
| deaths causally related to treatment / all      | 0 / 2              | 0 / 0              |  |
| Aortic valve disease                            |                    |                    |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)   | 1 / 9544 (0.01%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Aortic valve disease mixed                      |                    |                    |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)   | 1 / 9544 (0.01%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Aortic valve incompetence                       |                    |                    |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Aortic valve sclerosis                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arrhythmia                                      |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 1 / 1             | 0 / 0             |  |
| Aortic valve stenosis                           |                   |                   |  |
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 9 / 9544 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arrhythmia supraventricular                     |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriosclerosis coronary artery                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriospasm coronary                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Atrial flutter                                  |                   |                   |  |
| subjects affected / exposed                     | 49 / 9539 (0.51%) | 41 / 9544 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 52            | 0 / 45            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Atrial fibrillation                             |                   |                   |  |

|                                                 |                    |                    |
|-------------------------------------------------|--------------------|--------------------|
| subjects affected / exposed                     | 336 / 9539 (3.52%) | 232 / 9544 (2.43%) |
| occurrences causally related to treatment / all | 22 / 381           | 2 / 262            |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Atrial tachycardia                              |                    |                    |
| subjects affected / exposed                     | 4 / 9539 (0.04%)   | 5 / 9544 (0.05%)   |
| occurrences causally related to treatment / all | 0 / 4              | 0 / 5              |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Atrioventricular block                          |                    |                    |
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 0 / 9544 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 0              |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Atrioventricular block complete                 |                    |                    |
| subjects affected / exposed                     | 17 / 9539 (0.18%)  | 13 / 9544 (0.14%)  |
| occurrences causally related to treatment / all | 4 / 17             | 1 / 13             |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Atrioventricular block first degree             |                    |                    |
| subjects affected / exposed                     | 4 / 9539 (0.04%)   | 1 / 9544 (0.01%)   |
| occurrences causally related to treatment / all | 2 / 4              | 1 / 1              |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Atrioventricular block second degree            |                    |                    |
| subjects affected / exposed                     | 22 / 9539 (0.23%)  | 13 / 9544 (0.14%)  |
| occurrences causally related to treatment / all | 10 / 22            | 7 / 13             |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Atrioventricular dissociation                   |                    |                    |
| subjects affected / exposed                     | 0 / 9539 (0.00%)   | 1 / 9544 (0.01%)   |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Bradycardia                                     |                    |                    |
| subjects affected / exposed                     | 101 / 9539 (1.06%) | 21 / 9544 (0.22%)  |
| occurrences causally related to treatment / all | 91 / 102           | 15 / 21            |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |
| Bundle branch block                             |                    |                    |

|                                                 |                    |                    |  |
|-------------------------------------------------|--------------------|--------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Bundle branch block left                        |                    |                    |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%)   | 1 / 9544 (0.01%)   |  |
| occurrences causally related to treatment / all | 0 / 7              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Cardiac aneurysm                                |                    |                    |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)   | 9 / 9544 (0.09%)   |  |
| occurrences causally related to treatment / all | 0 / 5              | 0 / 9              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Cardiac arrest                                  |                    |                    |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%)  | 8 / 9544 (0.08%)   |  |
| occurrences causally related to treatment / all | 0 / 16             | 0 / 8              |  |
| deaths causally related to treatment / all      | 0 / 1              | 0 / 1              |  |
| Cardiac asthma                                  |                    |                    |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)   | 2 / 9544 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 2              | 0 / 2              |  |
| deaths causally related to treatment / all      | 0 / 1              | 0 / 0              |  |
| Cardiac failure                                 |                    |                    |  |
| subjects affected / exposed                     | 357 / 9539 (3.74%) | 346 / 9544 (3.63%) |  |
| occurrences causally related to treatment / all | 13 / 415           | 2 / 394            |  |
| deaths causally related to treatment / all      | 0 / 16             | 0 / 14             |  |
| Cardiac failure acute                           |                    |                    |  |
| subjects affected / exposed                     | 37 / 9539 (0.39%)  | 23 / 9544 (0.24%)  |  |
| occurrences causally related to treatment / all | 0 / 45             | 0 / 26             |  |
| deaths causally related to treatment / all      | 0 / 7              | 0 / 9              |  |
| Cardiac failure congestive                      |                    |                    |  |
| subjects affected / exposed                     | 31 / 9539 (0.32%)  | 24 / 9544 (0.25%)  |  |
| occurrences causally related to treatment / all | 0 / 33             | 0 / 26             |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 2              |  |
| Cardiac failure chronic                         |                    |                    |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 25 / 9539 (0.26%) | 29 / 9544 (0.30%) |  |
| occurrences causally related to treatment / all | 1 / 28            | 0 / 36            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Cardiac tamponade                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardio-respiratory arrest                       |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiogenic shock                               |                   |                   |  |
| subjects affected / exposed                     | 30 / 9539 (0.31%) | 22 / 9544 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 30            | 0 / 22            |  |
| deaths causally related to treatment / all      | 0 / 12            | 0 / 9             |  |
| Cardiomegaly                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiopulmonary failure                         |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Cardiomyopathy                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiovascular insufficiency                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 2             |  |
| Congestive cardiomyopathy                       |                   |                   |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Cor pulmonale                                   |                   |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Coronary artery disease                         |                   |                   |  |
| subjects affected / exposed                     | 20 / 9539 (0.21%) | 25 / 9544 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 21            | 0 / 25            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cor pulmonale chronic                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary artery dissection                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary artery insufficiency                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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                     | 14 / 9539 (0.15%) | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary artery stenosis                        |                   |                   |  |
| subjects affected / exposed                     | 18 / 9539 (0.19%) | 26 / 9544 (0.27%) |  |
| occurrences causally related to treatment / all | 0 / 19            | 0 / 26            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Coronary artery thrombosis                      |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dressler's syndrome                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocarditis noninfective                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Heart valve incompetence                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertensive heart disease                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intracardiac thrombus                           |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic cardiomyopathy                        |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Left atrial dilatation                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Left ventricular dysfunction                    |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| 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                     | 9 / 9539 (0.09%)  | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Left ventricular hypertrophy                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Low cardiac output syndrome                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Mitral valve incompetence                       |                   |                   |  |
| subjects affected / exposed                     | 16 / 9539 (0.17%) | 14 / 9544 (0.15%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Mitral valve prolapse                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Myocardial depression                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Myocardial fibrosis                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Myocardial infarction                           |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 98 / 9539 (1.03%) | 83 / 9544 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 104           | 0 / 88            |  |
| deaths causally related to treatment / all      | 0 / 15            | 0 / 14            |  |
| Myocardial ischaemia                            |                   |                   |  |
| subjects affected / exposed                     | 23 / 9539 (0.24%) | 27 / 9544 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 23            | 0 / 27            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Myocarditis                                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Nodal arrhythmia                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Nodal rhythm                                    |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 1 / 5             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Palpitations                                    |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pericardial effusion                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pericarditis                                    |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Postinfarction angina                           |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prinzmetal angina                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rhythm idioventricular                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 8 / 9539 (0.08%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Sick sinus syndrome                             |                  |                  |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 4 / 9            | 4 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Silent myocardial infarction                    |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinoatrial block                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus arrest                                    |                  |                  |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 8 / 9            | 4 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus arrhythmia                                |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 2 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sinus bradycardia                               |                   |                   |  |
| subjects affected / exposed                     | 48 / 9539 (0.50%) | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 42 / 49           | 4 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sinus tachycardia                               |                   |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%)  | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Supraventricular extrasystoles                  |                   |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%)  | 15 / 9544 (0.16%) |  |
| occurrences causally related to treatment / all | 1 / 8             | 2 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Supraventricular tachycardia                    |                   |                   |  |
| subjects affected / exposed                     | 17 / 9539 (0.18%) | 21 / 9544 (0.22%) |  |
| occurrences causally related to treatment / all | 1 / 18            | 0 / 24            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Supraventricular tachyarrhythmia                |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tachyarrhythmia                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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 / 9539 (0.02%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Torsade de pointes                              |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tricuspid valve incompetence                    |                   |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Trifascicular block                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ventricular arrhythmia                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Ventricular extrasystoles                       |                   |                   |  |
| subjects affected / exposed                     | 32 / 9539 (0.34%) | 21 / 9544 (0.22%) |  |
| occurrences causally related to treatment / all | 2 / 32            | 2 / 21            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ventricular failure                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Ventricular fibrillation                        |                   |                   |  |
| subjects affected / exposed                     | 20 / 9539 (0.21%) | 20 / 9544 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 22            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 6             |  |
| Ventricular tachycardia                         |                   |                   |  |
| subjects affected / exposed                     | 35 / 9539 (0.37%) | 21 / 9544 (0.22%) |  |
| occurrences causally related to treatment / all | 3 / 39            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Wolff-Parkinson-White syndrome                  |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nervous system disorders                        |                  |                  |  |
| Amnesia                                         |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Altered state of consciousness                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Amyotrophic lateral sclerosis                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anticholinergic syndrome                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aphasia                                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ataxia                                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Autonomic neuropathy                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Balance disorder                                |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain hypoxia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain injury                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain oedema                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain stem infarction                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid aneurysm rupture                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid arteriosclerosis                        |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid artery aneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carotid artery disease                          |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carotid artery dissection                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carotid artery occlusion                        |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carotid artery stenosis                         |                   |                   |  |
| subjects affected / exposed                     | 51 / 9539 (0.53%) | 43 / 9544 (0.45%) |  |
| occurrences causally related to treatment / all | 0 / 57            | 0 / 45            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carotid sinus syndrome                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carpal tunnel syndrome                          |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebellar atrophy                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebellar haemorrhage                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Cerebellar ischaemia                            |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebellar syndrome                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral arteriosclerosis                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral artery stenosis                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral atrophy                                |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral haematoma                              |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral haemorrhage                            |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Cerebral infarction                             |                   |                   |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Cerebral ischaemia                              |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 8 / 9539 (0.08%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral microangiopathy                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebrovascular accident                        |                   |                   |  |
| subjects affected / exposed                     | 31 / 9539 (0.32%) | 40 / 9544 (0.42%) |  |
| occurrences causally related to treatment / all | 0 / 32            | 0 / 44            |  |
| deaths causally related to treatment / all      | 0 / 5             | 0 / 5             |  |
| Cerebrovascular disorder                        |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebrovascular insufficiency                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cervical cord compression                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cervical myelopathy                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| 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 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cognitive disorder                              |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coma                                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Convulsion                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0            |  |
| Coordination abnormal                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cranial nerve disorder                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cranial nerve paralysis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cubital tunnel syndrome                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dementia                                        |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dementia Alzheimer's type                       |                  |                  |  |

|                                                  |                   |                   |  |
|--------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                      | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all  | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all       | 0 / 0             | 0 / 0             |  |
| Dementia of the Alzheimer's type, with delusions |                   |                   |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all  | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all       | 0 / 0             | 0 / 0             |  |
| Demyelinating polyneuropathy                     |                   |                   |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all  | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all       | 0 / 0             | 0 / 0             |  |
| Depressed level of consciousness                 |                   |                   |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all  | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all       | 0 / 0             | 0 / 0             |  |
| Diabetic hyperglycaemic coma                     |                   |                   |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all  | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all       | 0 / 1             | 0 / 0             |  |
| Diabetic neuropathy                              |                   |                   |  |
| subjects affected / exposed                      | 10 / 9539 (0.10%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all  | 0 / 10            | 0 / 10            |  |
| deaths causally related to treatment / all       | 0 / 0             | 0 / 0             |  |
| Dizziness                                        |                   |                   |  |
| subjects affected / exposed                      | 19 / 9539 (0.20%) | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all  | 3 / 19            | 3 / 20            |  |
| deaths causally related to treatment / all       | 0 / 0             | 0 / 0             |  |
| Dizziness postural                               |                   |                   |  |
| subjects affected / exposed                      | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all  | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all       | 0 / 0             | 0 / 0             |  |
| Drop attacks                                     |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dysarthria                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dystonic tremor                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encephalitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encephalomyelitis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encephalopathy                                  |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epilepsy                                        |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Essential tremor                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Extrapyramidal disorder                         |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Facial nerve disorder                           |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Grand mal convulsion                            |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Facial paresis                                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Guillain-Barre syndrome                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Haemorrhage intracranial                        |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Haemorrhagic stroke                             |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 4            | 0 / 5             |  |
| Headache                                        |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hemianopia homonymous                           |                  |                   |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hemiparesis                                     |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Horner's syndrome                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydrocephalus                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertensive encephalopathy                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoaesthesia                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 1 / 3            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemic coma                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hypoglycaemic unconsciousness                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyporeflexia                                    |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxic-ischaemic encephalopathy                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| IIIrd nerve paralysis                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intercostal neuralgia                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intracranial aneurysm                           |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intracranial hypotension                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intracranial pressure increased                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intracranial venous sinus thrombosis            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic cerebral infarction                   |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ischaemic neuropathy                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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                     | 97 / 9539 (1.02%) | 90 / 9544 (0.94%) |  |
| occurrences causally related to treatment / all | 1 / 100           | 0 / 95            |  |
| deaths causally related to treatment / all      | 0 / 13            | 0 / 6             |  |
| Lacunar infarction                              |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lethargy                                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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                     | 32 / 9539 (0.34%) | 22 / 9544 (0.23%) |  |
| occurrences causally related to treatment / all | 3 / 32            | 1 / 22            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lumbar radiculopathy                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Memory impairment                               |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Migraine                                        |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Monoplegia                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Movement disorder                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Multiple sclerosis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myasthenia gravis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myelitis transverse                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myelopathy                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nerve compression                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nerve root compression                          |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nerve root lesion                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuritis cranial                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neurodegenerative disorder                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neurological decompensation                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuropathy peripheral                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Normal pressure hydrocephalus                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paraesthesia                                    |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paraplegia                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parkinson's disease                             |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parkinsonism                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Partial seizures                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral sensorimotor neuropathy              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral sensory neuropathy                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polyneuropathy                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Petit mal epilepsy                              |                  |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Poor quality sleep                              |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Post-injection delirium sedation syndrome       |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Post-traumatic headache                         |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Presyncope                                      |                   |                  |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 4 / 15            | 1 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Posterior reversible encephalopathy syndrome    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Psychomotor hyperactivity                       |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pyramidal tract syndrome                        |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Radial nerve compression                        |                   |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radicular pain                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radicular syndrome                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radiculopathy                                   |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Restless legs syndrome                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retrograde amnesia                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sciatica                                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Senile dementia                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Speech disorder                                 |                  |                  |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Somnolence                                      |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 1 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spinal cord compression                         |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spinal vascular disorder                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spondylitic myelopathy                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Subdural hygroma                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Syncope                                         |                   |                   |  |
| subjects affected / exposed                     | 91 / 9539 (0.95%) | 89 / 9544 (0.93%) |  |
| occurrences causally related to treatment / all | 23 / 102          | 6 / 96            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Thalamic infarction                             |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Thalamus haemorrhage                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Thrombotic stroke                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tonic convulsion                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Transient global amnesia                        |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tremor                                          |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Transient ischaemic attack                      |                   |                   |  |
| subjects affected / exposed                     | 56 / 9539 (0.59%) | 50 / 9544 (0.52%) |  |
| occurrences causally related to treatment / all | 3 / 59            | 0 / 50            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ulnar neurapraxia                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ulnar tunnel syndrome                           |                   |                   |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| VIIth nerve paralysis                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| VIth nerve disorder                             |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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 / 9539 (0.00%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vascular dementia                               |                   |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vascular encephalopathy                         |                   |                  |  |
| subjects affected / exposed                     | 11 / 9539 (0.12%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vertebral artery occlusion                      |                   |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vertebral artery stenosis                       |                   |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vertebrobasilar insufficiency                   |                   |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vertigo CNS origin                              |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vocal cord paresis                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Wernicke-Korsakoff syndrome                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood and lymphatic system disorders            |                   |                   |  |
| Agranulocytosis                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Anaemia                                         |                   |                   |  |
| subjects affected / exposed                     | 30 / 9539 (0.31%) | 45 / 9544 (0.47%) |  |
| occurrences causally related to treatment / all | 0 / 30            | 0 / 45            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Anaemia folate deficiency                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Anaemia megaloblastic                           |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Anaemia vitamin B12 deficiency                  |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bone marrow failure                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Deficiency anaemia                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Disseminated intravascular coagulation          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Febrile neutropenia                             |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Haemorrhagic diathesis                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haemorrhagic anaemia                            |                   |                   |  |
| subjects affected / exposed                     | 14 / 9539 (0.15%) | 15 / 9544 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haemorrhagic disorder                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Heparin-induced thrombocytopenia                |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypochromic anaemia                             |                  |                  |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoprothrombinaemia                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Idiopathic thrombocytopenic purpura             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leukocytosis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Iron deficiency anaemia                         |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leukopenia                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphadenopathy                                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphadenopathy mediastinal                     |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphopenia                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Microcytic anaemia                              |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrogenic anaemia                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neutropenia                                     |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Normochromic normocytic anaemia                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancytopenia                                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Platelet dysfunction                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sideroblastic anaemia                           |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Thrombocytopenia                                |                   |                   |  |
| subjects affected / exposed                     | 15 / 9539 (0.16%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 17            | 1 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Thrombocytopenic purpura                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Thrombocytosis                                  |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ear and labyrinth disorders                     |                   |                   |  |
| Acute vestibular syndrome                       |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Deafness neurosensory                           |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Deafness unilateral                             |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haematotympanum                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hearing impaired                                |                   |                   |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoacusis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Meniere's disease                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neurosensory hypoacusis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sudden hearing loss                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tinnitus                                        |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tympanic membrane disorder                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vertigo                                         |                  |                  |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 2 / 9            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vestibular ataxia                               |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vestibular disorder                             |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Eye disorders                                   |                   |                   |  |
| Age-related macular degeneration                |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Amaurosis                                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Amaurosis fugax                                 |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Angle closure glaucoma                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blindness                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cataract                                        |                   |                   |  |
| subjects affected / exposed                     | 39 / 9539 (0.41%) | 32 / 9544 (0.34%) |  |
| occurrences causally related to treatment / all | 0 / 43            | 0 / 32            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blindness unilateral                            |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cataract diabetic                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cataract nuclear                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cataract subcapsular                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Choroidal effusion                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Choroidal neovascularisation                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Conjunctival haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dacryoadenitis acquired                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dacryostenosis acquired                         |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic glaucoma                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic retinal oedema                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic retinopathy                            |                   |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%)  | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diplopia                                        |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 1 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Eye haemorrhage                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Glaucoma                                        |                   |                   |  |
| subjects affected / exposed                     | 20 / 9539 (0.21%) | 19 / 9544 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Glaucomatous optic disc atrophy                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Keratitis                                       |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Macular degeneration                            |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Macular fibrosis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Normal tension glaucoma                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ocular hypertension                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ocular icterus                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Open angle glaucoma                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Optic atrophy                                   |                  |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Ophthalmoplegia                                 |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Optic ischaemic neuropathy                      |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Papilloedema                                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Periorbital oedema                              |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Photophobia                                     |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Pterygium                                       |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Photopsia                                       |                   |                  |  |
| subjects affected / exposed                     | 28 / 9539 (0.29%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 29 / 31           | 2 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal aneurysm                                |                   |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal artery occlusion                        |                   |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal artery thrombosis                       |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal detachment                              |                   |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal haemorrhage                             |                   |                  |  |
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal tear                                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal vascular thrombosis                     |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal vein occlusion                          |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal vein thrombosis                         |                   |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinopathy haemorrhagic                        |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinopathy hypertensive                        |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinoschisis                                   |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vision blurred                                  |                   |                  |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 11 / 14           | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Visual acuity reduced                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Visual impairment                               |                   |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 2 / 3             | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vitreous detachment                             |                   |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vitreous floaters                               |                   |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vitreous haemorrhage                            |                  |                  |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 10           | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal disorders                      |                  |                  |  |
| Abdominal adhesions                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal discomfort                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal distension                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal hernia                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal hernia obstructive                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal pain                                  |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal pain upper                            |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal rigidity                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal strangulated hernia                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acquired oesophageal web                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute abdomen                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal fissure                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal fistula                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal polyp                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal ulcer                                      |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ascites                                         |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Barrett's oesophagus                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis                                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis ischaemic                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Colitis ulcerative                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colonic pseudo-obstruction                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colonic stenosis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Constipation                                    |                  |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Crohn's disease                                 |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Dental alveolar anomaly                         |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic gastroparesis                          |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diaphragmatic hernia                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diarrhoea                                       |                   |                  |  |
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 1 / 10            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diarrhoea haemorrhagic                          |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diverticular perforation                        |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diverticulitis intestinal haemorrhagic          |                   |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum intestinal                         |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dry mouth                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum intestinal haemorrhagic            |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal obstruction                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Duodenal polyp                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal ulcer                                  |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal ulcer haemorrhage                      |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Duodenal ulcer perforation                      |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Duodenitis haemorrhagic                         |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Duodenitis                                      |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Dyspepsia                                       |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Dysphagia                                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Enteritis                                       |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Enterocolitis                                   |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Enterocolitis haemorrhagic                      |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epigastric discomfort                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erosive duodenitis                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erosive oesophagitis                            |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Faecal incontinence                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Flatulence                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Functional gastrointestinal disorder            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric haemorrhage                             |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Gastric mucosa erythema                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastric polyps                                  |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastric ulcer                                   |                   |                   |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%)  | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastric ulcer haemorrhage                       |                   |                   |  |
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 15 / 9544 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastric ulcer perforation                       |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Gastric varices                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastric varices haemorrhage                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastritis                                       |                   |                   |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 14 / 9539 (0.15%) | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastritis atrophic                              |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastritis erosive                               |                   |                   |  |
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastritis haemorrhagic                          |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroduodenal haemorrhage                      |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroduodenitis                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroduodenitis haemorrhagic                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrointestinal angiodysplasia                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrointestinal angiodysplasia haemorrhagic    |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrointestinal dysplasia                      |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrointestinal erosion                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrointestinal haemorrhage                    |                   |                   |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 13            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Gastrooesophageal reflux disease                |                   |                   |  |
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 9 / 9544 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrooesophagitis                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haematemesis                                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haematochezia                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Haemorrhagic erosive gastritis                  |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoidal haemorrhage                       |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoids                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hernial eventration                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hiatus hernia                                   |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileal stenosis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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 / 9539 (0.03%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Ileus paralytic                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Impaired gastric emptying                       |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Inguinal hernia                                 |                   |                   |  |
| subjects affected / exposed                     | 29 / 9539 (0.30%) | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 31            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Inguinal hernia strangulated                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Inguinal hernia, obstructive                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intestinal angina                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intestinal fistula                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intestinal haemorrhage                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intestinal ischaemia                            |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intestinal mass                                 |                   |                   |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intestinal obstruction                          |                   |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intestinal polyp                                |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Intestinal polyp haemorrhage                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Irritable bowel syndrome                        |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Large intestinal haemorrhage                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Large intestine perforation                     |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Large intestine polyp                           |                   |                  |  |
| subjects affected / exposed                     | 11 / 9539 (0.12%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Leukoplakia oral                                |                   |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lip swelling                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lower gastrointestinal haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mallory-Weiss syndrome                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mechanical ileus                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Melaena                                         |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesenteric artery thrombosis                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Mesenteric haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesenteric occlusion                            |                  |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Mikulicz's disease                              |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Nausea                                          |                   |                  |  |
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Oedematous pancreatitis                         |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Oesophageal achalasia                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Oesophageal stenosis                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Oesophageal ulcer haemorrhage                   |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Oesophageal varices haemorrhage                 |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Oesophagitis                                    |                   |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Oesophagitis haemorrhagic                       |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Oesophagitis ulcerative                         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Oral submucosal fibrosis                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pancreatic pseudocyst                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pancreatitis                                    |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pancreatitis acute                              |                   |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%)  | 17 / 9544 (0.18%) |  |
| occurrences causally related to treatment / all | 1 / 9             | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Pancreatitis chronic                            |                   |                   |  |
| subjects affected / exposed                     | 11 / 9539 (0.12%) | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peptic ulcer                                    |                   |                   |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peptic ulcer haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periproctitis                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Proctitis ulcerative                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal haemorrhage                              |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal polyp                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal prolapse                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal ulcer haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Reflux gastritis                                |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retching                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal haemorrhage                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland calculus                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sigmoiditis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestinal obstruction                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestinal perforation                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenic artery aneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subileus                                        |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Swollen tongue                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombosis mesenteric vessel                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Tongue ulceration                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Umbilical hernia                                |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Umbilical hernia, obstructive                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper gastrointestinal haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 8 / 9539 (0.08%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Varices oesophageal                             |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Volvulus                                        |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Vomiting                                        |                  |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 1 / 9            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Skin and subcutaneous tissue disorders          |                  |                   |  |
| Angioedema                                      |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 3 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cold sweat                                      |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Decubitus ulcer                                 |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Dermatitis                                      |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Dermatitis allergic                             |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Dermatitis bullous                              |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Dermatomyositis                                 |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 4 / 9539 (0.04%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dry gangrene                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ecchymosis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eczema                                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erythema                                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hidradenitis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperhidrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 1 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Keloid scar                                     |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leukocytoclastic vasculitis                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lichen planus                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Necrobiosis lipoidica diabetorum                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuropathic ulcer                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Panniculitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parapsoriasis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pruritus                                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pemphigus                                       |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pruritus allergic                               |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Psoriasis                                       |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Purpura                                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Rash generalised                                |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Skin lesion                                     |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Skin necrosis                                   |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Skin ulcer                                      |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Skin ulcer haemorrhage                          |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Swelling face                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxic skin eruption                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urticaria                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 2 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal and urinary disorders                     |                  |                  |  |
| Acute prerenal failure                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anuria                                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder dilatation                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder diverticulum                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder neck sclerosis                          |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder prolapse                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder perforation                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder stenosis                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder tamponade                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Calculus bladder                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Calculus ureteric                               |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Calculus urethral                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Calculus urinary                                |                  |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cystitis glandularis                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cystitis haemorrhagic                           |                   |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Cystitis noninfective                           |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic nephropathy                            |                   |                  |  |
| subjects affected / exposed                     | 11 / 9539 (0.12%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Dysuria                                         |                   |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Glomerulonephritis                              |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Haematuria                                      |                   |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%)  | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Hydronephrosis                                  |                   |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hydroureter                                     |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hypertensive nephropathy                        |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hypertonic bladder                              |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| IgA nephropathy                                 |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Incontinence                                    |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Nephroangiosclerosis                            |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Nephrolithiasis                                 |                  |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 14 / 9544 (0.15%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Nephropathy                                     |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephropathy toxic                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrotic syndrome                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Obstructive uropathy                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 1 / 9539 (0.01%) | 0 / 9544 (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 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal artery occlusion                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal artery stenosis                           |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal artery thrombosis                         |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal colic                                     |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal cyst                                      |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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                     | 38 / 9539 (0.40%) | 30 / 9544 (0.31%) |  |
| occurrences causally related to treatment / all | 1 / 39            | 0 / 30            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 3             |  |
| Renal failure acute                             |                   |                   |  |
| subjects affected / exposed                     | 29 / 9539 (0.30%) | 35 / 9544 (0.37%) |  |
| occurrences causally related to treatment / all | 0 / 31            | 0 / 38            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Renal failure chronic                           |                   |                   |  |
| subjects affected / exposed                     | 34 / 9539 (0.36%) | 17 / 9544 (0.18%) |  |
| occurrences causally related to treatment / all | 1 / 35            | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Renal impairment                                |                   |                   |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%) | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal infarct                                   |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal ischaemia                                 |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal tubular acidosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stress urinary incontinence                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tubulointerstitial nephritis                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureteric obstruction                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urethral disorder                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urethral obstruction                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urethral stenosis                               |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary bladder haemorrhage                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary bladder polyp                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary incontinence                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary retention                               |                   |                   |  |
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract obstruction                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vesicoureteric reflux                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Endocrine disorders                             |                   |                   |  |
| Autoimmune thyroiditis                          |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Adrenal insufficiency                           |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Basedow's disease                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cushing's syndrome                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Empty sella syndrome                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Goitre                                          |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperthyroidism                                 |                  |                  |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 5 / 9544 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypothyroidism                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Inappropriate antidiuretic hormone secretion    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxic nodular goitre                            |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal and connective tissue disorders |                  |                  |  |
| Amyotrophy                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ankylosing spondylitis                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthralgia                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bursitis                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Back pain                                       |                  |                  |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| CREST syndrome                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervical spinal stenosis                        |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chondrocalcinosis pyrophosphate                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chondromalacia                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chondropathy                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Costochondritis                                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dupuytren's contracture                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Exostosis of jaw                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fasciitis                                       |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fistula                                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Foot deformity                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gouty arthritis                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gouty tophus                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Groin pain                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemarthrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral disc compression                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intervertebral disc disorder                    |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intervertebral disc displacement                |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Intervertebral disc protrusion                  |                   |                   |  |
| subjects affected / exposed                     | 12 / 9539 (0.13%) | 20 / 9544 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Kyphosis                                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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                     | 9 / 9539 (0.09%)  | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Mobility decreased                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Muscle haemorrhage                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Muscle tightness                                |                   |                   |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Muscular weakness                               |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Musculoskeletal chest pain                      |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Musculoskeletal pain                            |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Musculoskeletal stiffness                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Myopathy                                        |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Myopathy toxic                                  |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Neck pain                                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Neuropathic arthropathy                         |                  |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteitis                                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteoarthritis                                  |                   |                   |  |
| subjects affected / exposed                     | 46 / 9539 (0.48%) | 43 / 9544 (0.45%) |  |
| occurrences causally related to treatment / all | 0 / 47            | 0 / 48            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteochondritis                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteochondrosis                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteonecrosis                                   |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteoporosis                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteoporosis postmenopausal                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Osteoporotic fracture                           |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (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                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Patellofemoral pain syndrome                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periarthritis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polymyalgia rheumatica                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pseudarthrosis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psoriatic arthropathy                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rhabdomyolysis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rheumatoid arthritis                            |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Rotator cuff syndrome                           |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Scoliosis                                       |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spinal column stenosis                          |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spinal osteoarthritis                           |                   |                   |  |
| subjects affected / exposed                     | 18 / 9539 (0.19%) | 16 / 9544 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 18            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Spondyloarthropathy                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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 / 9539 (0.02%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sympathetic posterior cervical syndrome         |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Synovitis                                       |                   |                   |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Systemic sclerosis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tenosynovitis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vertebral foraminal stenosis                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| Abdominal wall abscess                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess jaw                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess limb                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute hepatitis C                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute sinusitis                                 |                  |                  |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Anal abscess                                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Anal candidiasis                                |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Appendiceal abscess                             |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Appendicitis                                    |                   |                  |  |
| subjects affected / exposed                     | 16 / 9539 (0.17%) | 9 / 9544 (0.09%) |  |
| occurrences causally related to treatment / all | 0 / 18            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Appendicitis perforated                         |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Arteriosclerotic gangrene                       |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Arteriovenous graft site infection              |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Arthritis bacterial                             |                   |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atypical pneumonia                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacteraemia                                     |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial diarrhoea                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial infection                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial prostatitis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Biliary tract infection                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Borrelia infection                              |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Brain abscess                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchiolitis                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchitis                                      |                   |                   |  |
| subjects affected / exposed                     | 16 / 9539 (0.17%) | 22 / 9544 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchopneumonia                                |                   |                   |  |
| subjects affected / exposed                     | 29 / 9539 (0.30%) | 24 / 9544 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 33            | 0 / 26            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 2             |  |
| Bronchitis bacterial                            |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchopulmonary aspergillosis                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Campylobacter gastroenteritis                   |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Candida pneumonia                               |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Candidiasis                                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carbuncle                                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cellulitis                                      |                   |                   |  |
| subjects affected / exposed                     | 23 / 9539 (0.24%) | 18 / 9544 (0.19%) |  |
| occurrences causally related to treatment / all | 0 / 23            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cellulitis gangrenous                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cervicitis                                      |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholangitis suppurative                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholecystitis infective                         |                   |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chronic hepatitis C                             |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic sinusitis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystitis                                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridium difficile colitis                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Cystitis klebsiella                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dengue fever                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device related infection                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 4 / 9544 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic foot infection                         |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic gangrene                               |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Diarrhoea infectious                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Diverticulitis                                  |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Ear infection                                   |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Echinococciasis                                 |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Emphysematous cholecystitis                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Empyema                                         |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Endocarditis                                    |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Endocarditis bacterial                          |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Endocarditis enterococcal                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocarditis staphylococcal                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Enterobacter sepsis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterococcal sepsis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis bacterial                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis infectious                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epiglottitis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erysipelas                                      |                  |                  |  |



|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 20 / 9539 (0.21%) | 15 / 9544 (0.16%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Escherichia infection                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Escherichia urinary tract infection             |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Folliculitis                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gallbladder empyema                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gangrene                                        |                   |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Gastroenteritis                                 |                   |                   |  |
| subjects affected / exposed                     | 16 / 9539 (0.17%) | 16 / 9544 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroenteritis bacterial                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastroenteritis clostridial                     |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis salmonella                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis shigella                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis viral                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal bacterial infection            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal viral infection                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Groin abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemophilus infection                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Helicobacter gastritis                          |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Helicobacter infection                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis A                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis B                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatitis C                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster infection neurological            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster ophthalmic                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster oticus                            |                  |                  |  |

|                                                               |                  |                  |  |
|---------------------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                                   | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infected cyst                                                 |                  |                  |  |
| subjects affected / exposed                                   | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infected dermal cyst                                          |                  |                  |  |
| subjects affected / exposed                                   | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infected skin ulcer                                           |                  |                  |  |
| subjects affected / exposed                                   | 0 / 9539 (0.00%) | 3 / 9544 (0.03%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infection                                                     |                  |                  |  |
| subjects affected / exposed                                   | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all               | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infectious pleural effusion                                   |                  |                  |  |
| subjects affected / exposed                                   | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infective exacerbation of bronchiectasis                      |                  |                  |  |
| subjects affected / exposed                                   | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all               | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infective exacerbation of chronic obstructive airways disease |                  |                  |  |
| subjects affected / exposed                                   | 5 / 9539 (0.05%) | 6 / 9544 (0.06%) |  |
| occurrences causally related to treatment / all               | 0 / 5            | 0 / 7            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infective myositis                                            |                  |                  |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Influenza                                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injection site abscess                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral discitis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Keratitis herpetic                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngitis                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngitis bacterial                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laryngitis fungal                               |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Legionella infection                            |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Liver abscess                                   |                  |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lobar pneumonia                                 |                  |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Localised infection                             |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lower respiratory tract infection               |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 9 / 9544 (0.09%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lower respiratory tract infection bacterial     |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lung abscess                                    |                  |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lung infection                                  |                  |                   |  |

|                                                 |                   |                  |  |
|-------------------------------------------------|-------------------|------------------|--|
| subjects affected / exposed                     | 11 / 9539 (0.12%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 11           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Lyme disease                                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Lymphangitis                                    |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Malaria                                         |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Mastoiditis                                     |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Mediastinal abscess                             |                   |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Mediastinitis                                   |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Meningitis                                      |                   |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Meningitis tuberculous                          |                   |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Meningitis viral                                |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Muscle abscess                                  |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Necrotising fasciitis                           |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Oesophageal candidiasis                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Orchitis                                        |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Osteomyelitis                                   |                  |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Osteomyelitis bacterial                         |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Osteomyelitis chronic                           |                  |                   |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media acute                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media chronic                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic abscess                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perihepatic abscess                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perineal abscess                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periodontitis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritoneal abscess                              |                  |                  |  |

|                                                 |                    |                    |  |
|-------------------------------------------------|--------------------|--------------------|--|
| subjects affected / exposed                     | 2 / 9539 (0.02%)   | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 2              | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Peritonitis                                     |                    |                    |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%)   | 9 / 9544 (0.09%)   |  |
| occurrences causally related to treatment / all | 0 / 9              | 0 / 9              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 2              |  |
| Peritonitis bacterial                           |                    |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Peritonsillar abscess                           |                    |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Pertussis                                       |                    |                    |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)   | 1 / 9544 (0.01%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Pharyngitis                                     |                    |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Pneumococcal sepsis                             |                    |                    |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)   | 0 / 9544 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Pneumonia                                       |                    |                    |  |
| subjects affected / exposed                     | 122 / 9539 (1.28%) | 102 / 9544 (1.07%) |  |
| occurrences causally related to treatment / all | 0 / 129            | 0 / 112            |  |
| deaths causally related to treatment / all      | 0 / 6              | 0 / 3              |  |
| Pneumonia bacterial                             |                    |                    |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 7 / 9544 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Pneumonia escherichia                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia haemophilus                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia klebsiella                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia moraxella                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia mycoplasmal                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia pneumococcal                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia pseudomonas aeruginosa                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia streptococcal                         |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pneumonia viral                                 |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Post procedural cellulitis                      |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Post procedural infection                       |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Post procedural sepsis                          |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Postoperative abscess                           |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Postoperative wound infection                   |                  |                   |  |
| subjects affected / exposed                     | 6 / 9539 (0.06%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pseudomembranous colitis                        |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pseudomonal bacteraemia                         |                  |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary tuberculoma                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary tuberculosis                          |                  |                  |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Puncture site abscess                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Puncture site infection                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyelonephritis                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyelonephritis acute                            |                  |                  |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 8 / 9544 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyelonephritis chronic                          |                  |                  |  |

|                                                 |                  |                   |  |
|-------------------------------------------------|------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 9539 (0.07%) | 6 / 9544 (0.06%)  |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pyoderma                                        |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pyonephrosis                                    |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Renal tuberculosis                              |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Respiratory syncytial virus infection           |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Respiratory moniliasis                          |                  |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Respiratory tract infection                     |                  |                   |  |
| subjects affected / exposed                     | 5 / 9539 (0.05%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Respiratory tract infection bacterial           |                  |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Respiratory tract infection viral               |                  |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Salmonellosis                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sepsis                                          |                   |                   |  |
| subjects affected / exposed                     | 11 / 9539 (0.12%) | 11 / 9544 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 5             | 0 / 3             |  |
| Scrotal abscess                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Septic arthritis staphylococcal                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Septic shock                                    |                   |                   |  |
| subjects affected / exposed                     | 9 / 9539 (0.09%)  | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 6             | 0 / 5             |  |
| Sinusitis                                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Skin infection                                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Small intestine gangrene                        |                   |                   |  |

|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Sputum purulent                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Staphylococcal infection                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Staphylococcal osteomyelitis                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Staphylococcal sepsis                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Streptococcal sepsis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| 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                     | 4 / 9539 (0.04%) | 2 / 9544 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Systemic candida                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tonsillitis bacterial                           |                  |                  |  |



|                                                 |                  |                  |  |
|-------------------------------------------------|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tooth infection                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxic shock syndrome                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%) | 1 / 9544 (0.01%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tracheobronchitis                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tuberculosis gastrointestinal                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tuberculous pleurisy                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tubo-ovarian abscess                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Typhoid fever                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%) | 0 / 9544 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper respiratory tract infection               |                  |                  |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 6 / 9539 (0.06%)  | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection                         |                   |                   |  |
| subjects affected / exposed                     | 26 / 9539 (0.27%) | 17 / 9544 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection bacterial               |                   |                   |  |
| subjects affected / exposed                     | 7 / 9539 (0.07%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection enterococcal            |                   |                   |  |
| subjects affected / exposed                     | 2 / 9539 (0.02%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urosepsis                                       |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 13 / 9544 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Viral infection                                 |                   |                   |  |
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Viral pericarditis                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Wound infection                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Wound infection bacterial                       |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 3 / 9539 (0.03%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Wound infection pseudomonas                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Metabolism and nutrition disorders              |                   |                   |  |
| Acidosis                                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (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                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Decreased appetite                              |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 1 / 4             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Dehydration                                     |                   |                   |  |
| subjects affected / exposed                     | 19 / 9539 (0.20%) | 19 / 9544 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetes mellitus                               |                   |                   |  |
| subjects affected / exposed                     | 59 / 9539 (0.62%) | 82 / 9544 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 65            | 0 / 87            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Diabetes mellitus inadequate control            |                   |                   |  |
| subjects affected / exposed                     | 34 / 9539 (0.36%) | 50 / 9544 (0.52%) |  |
| occurrences causally related to treatment / all | 0 / 36            | 0 / 53            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic complication                           |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic ketoacidosis                           |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Fluid retention                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gout                                            |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 3 / 9544 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypercholesterolaemia                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyperglycaemia                                  |                   |                   |  |
| subjects affected / exposed                     | 10 / 9539 (0.10%) | 4 / 9544 (0.04%)  |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyperkalaemia                                   |                   |                   |  |
| subjects affected / exposed                     | 13 / 9539 (0.14%) | 10 / 9544 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypertriglyceridaemia                           |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypocalcaemia                                   |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypoglycaemia                                   |                   |                   |  |
| subjects affected / exposed                     | 19 / 9539 (0.20%) | 12 / 9544 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypokalaemia                                    |                   |                   |  |
| subjects affected / exposed                     | 4 / 9539 (0.04%)  | 5 / 9544 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypomagnesaemia                                 |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyponatraemia                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 7 / 9544 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypoproteinaemia                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Insulin-requiring type 2 diabetes mellitus      |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ketoacidosis                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Lactic acidosis                                 |                   |                   |  |

|                                                 |                   |                   |  |
|-------------------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Malnutrition                                    |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| 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 / 9539 (0.01%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Metabolic alkalosis                             |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 2 / 9544 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Obesity                                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 9539 (0.00%)  | 1 / 9544 (0.01%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Type 1 diabetes mellitus                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Type 2 diabetes mellitus                        |                   |                   |  |
| subjects affected / exposed                     | 25 / 9539 (0.26%) | 47 / 9544 (0.49%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 0 / 52            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Type 3 diabetes mellitus                        |                   |                   |  |
| subjects affected / exposed                     | 1 / 9539 (0.01%)  | 0 / 9544 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

Frequency threshold for reporting non-serious adverse events: 1 %

| <b>Non-serious adverse events</b>                     | Ivabradine              | Placebo                 |  |
|-------------------------------------------------------|-------------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events |                         |                         |  |
| subjects affected / exposed                           | 6920 / 9539<br>(72.54%) | 6321 / 9544<br>(66.23%) |  |
| Vascular disorders                                    |                         |                         |  |
| Hypertensive crisis                                   |                         |                         |  |
| subjects affected / exposed                           | 129 / 9539 (1.35%)      | 140 / 9544 (1.47%)      |  |
| occurrences (all)                                     | 147                     | 160                     |  |
| Hypertension                                          |                         |                         |  |
| subjects affected / exposed                           | 1129 / 9539<br>(11.84%) | 923 / 9544 (9.67%)      |  |
| occurrences (all)                                     | 1322                    | 1070                    |  |
| Hypotension                                           |                         |                         |  |
| subjects affected / exposed                           | 178 / 9539 (1.87%)      | 190 / 9544 (1.99%)      |  |
| occurrences (all)                                     | 187                     | 198                     |  |
| Peripheral arterial occlusive disease                 |                         |                         |  |
| subjects affected / exposed                           | 122 / 9539 (1.28%)      | 128 / 9544 (1.34%)      |  |
| occurrences (all)                                     | 131                     | 135                     |  |
| General disorders and administration site conditions  |                         |                         |  |
| Chest pain                                            |                         |                         |  |
| subjects affected / exposed                           | 108 / 9539 (1.13%)      | 132 / 9544 (1.38%)      |  |
| occurrences (all)                                     | 121                     | 158                     |  |
| Non-cardiac chest pain                                |                         |                         |  |
| subjects affected / exposed                           | 119 / 9539 (1.25%)      | 114 / 9544 (1.19%)      |  |
| occurrences (all)                                     | 131                     | 123                     |  |
| Fatigue                                               |                         |                         |  |
| subjects affected / exposed                           | 126 / 9539 (1.32%)      | 110 / 9544 (1.15%)      |  |
| occurrences (all)                                     | 131                     | 116                     |  |
| Oedema peripheral                                     |                         |                         |  |
| subjects affected / exposed                           | 214 / 9539 (2.24%)      | 170 / 9544 (1.78%)      |  |
| occurrences (all)                                     | 234                     | 178                     |  |
| Reproductive system and breast disorders              |                         |                         |  |
| Benign prostatic hyperplasia                          |                         |                         |  |
| subjects affected / exposed                           | 121 / 9539 (1.27%)      | 132 / 9544 (1.38%)      |  |
| occurrences (all)                                     | 121                     | 132                     |  |

|                                                 |                      |                    |  |
|-------------------------------------------------|----------------------|--------------------|--|
| Respiratory, thoracic and mediastinal disorders |                      |                    |  |
| Chronic obstructive pulmonary disease           |                      |                    |  |
| subjects affected / exposed                     | 168 / 9539 (1.76%)   | 152 / 9544 (1.59%) |  |
| occurrences (all)                               | 211                  | 198                |  |
| Cough                                           |                      |                    |  |
| subjects affected / exposed                     | 154 / 9539 (1.61%)   | 138 / 9544 (1.45%) |  |
| occurrences (all)                               | 165                  | 146                |  |
| Dyspnoea                                        |                      |                    |  |
| subjects affected / exposed                     | 136 / 9539 (1.43%)   | 114 / 9544 (1.19%) |  |
| occurrences (all)                               | 144                  | 121                |  |
| Psychiatric disorders                           |                      |                    |  |
| Insomnia                                        |                      |                    |  |
| subjects affected / exposed                     | 100 / 9539 (1.05%)   | 99 / 9544 (1.04%)  |  |
| occurrences (all)                               | 102                  | 102                |  |
| Investigations                                  |                      |                    |  |
| Blood pressure increased                        |                      |                    |  |
| subjects affected / exposed                     | 118 / 9539 (1.24%)   | 117 / 9544 (1.23%) |  |
| occurrences (all)                               | 145                  | 145                |  |
| Blood creatinine increased                      |                      |                    |  |
| subjects affected / exposed                     | 114 / 9539 (1.20%)   | 88 / 9544 (0.92%)  |  |
| occurrences (all)                               | 118                  | 89                 |  |
| C-reactive protein increased                    |                      |                    |  |
| subjects affected / exposed                     | 155 / 9539 (1.62%)   | 140 / 9544 (1.47%) |  |
| occurrences (all)                               | 159                  | 143                |  |
| Electrocardiogram QT prolonged                  |                      |                    |  |
| subjects affected / exposed                     | 161 / 9539 (1.69%)   | 58 / 9544 (0.61%)  |  |
| occurrences (all)                               | 178                  | 62                 |  |
| Heart rate decreased                            |                      |                    |  |
| subjects affected / exposed                     | 1032 / 9539 (10.82%) | 112 / 9544 (1.17%) |  |
| occurrences (all)                               | 1173                 | 123                |  |
| Injury, poisoning and procedural complications  |                      |                    |  |
| Fall                                            |                      |                    |  |
| subjects affected / exposed                     | 259 / 9539 (2.72%)   | 287 / 9544 (3.01%) |  |
| occurrences (all)                               | 284                  | 313                |  |
| Cardiac disorders                               |                      |                    |  |



|                                                                                         |                           |                           |
|-----------------------------------------------------------------------------------------|---------------------------|---------------------------|
| Acute myocardial infarction<br>subjects affected / exposed<br>occurrences (all)         | 200 / 9539 (2.10%)<br>216 | 208 / 9544 (2.18%)<br>229 |
| Angina pectoris<br>subjects affected / exposed<br>occurrences (all)                     | 611 / 9539 (6.41%)<br>684 | 692 / 9544 (7.25%)<br>774 |
| Angina unstable<br>subjects affected / exposed<br>occurrences (all)                     | 412 / 9539 (4.32%)<br>482 | 436 / 9544 (4.57%)<br>527 |
| Atrioventricular block first degree<br>subjects affected / exposed<br>occurrences (all) | 251 / 9539 (2.63%)<br>269 | 204 / 9544 (2.14%)<br>222 |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                 | 438 / 9539 (4.59%)<br>538 | 316 / 9544 (3.31%)<br>370 |
| Cardiac failure<br>subjects affected / exposed<br>occurrences (all)                     | 469 / 9539 (4.92%)<br>546 | 464 / 9544 (4.86%)<br>531 |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)                         | 569 / 9539 (5.96%)<br>613 | 77 / 9544 (0.81%)<br>84   |
| Myocardial infarction<br>subjects affected / exposed<br>occurrences (all)               | 98 / 9539 (1.03%)<br>104  | 83 / 9544 (0.87%)<br>88   |
| Sinus bradycardia<br>subjects affected / exposed<br>occurrences (all)                   | 189 / 9539 (1.98%)<br>199 | 22 / 9544 (0.23%)<br>24   |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)                   | 46 / 9539 (0.48%)<br>46   | 170 / 9544 (1.78%)<br>193 |
| Supraventricular extrasystoles<br>subjects affected / exposed<br>occurrences (all)      | 184 / 9539 (1.93%)<br>194 | 143 / 9544 (1.50%)<br>144 |
| Ventricular extrasystoles<br>subjects affected / exposed<br>occurrences (all)           | 335 / 9539 (3.51%)<br>363 | 264 / 9544 (2.77%)<br>288 |

|                                      |                             |                    |                    |
|--------------------------------------|-----------------------------|--------------------|--------------------|
| Nervous system disorders             |                             |                    |                    |
|                                      | Dizziness                   |                    |                    |
|                                      | subjects affected / exposed | 291 / 9539 (3.05%) | 217 / 9544 (2.27%) |
|                                      | occurrences (all)           | 311                | 235                |
| Headache                             |                             |                    |                    |
|                                      | subjects affected / exposed | 170 / 9539 (1.78%) | 146 / 9544 (1.53%) |
|                                      | occurrences (all)           | 195                | 162                |
| Ischaemic stroke                     |                             |                    |                    |
|                                      | subjects affected / exposed | 97 / 9539 (1.02%)  | 90 / 9544 (0.94%)  |
|                                      | occurrences (all)           | 100                | 95                 |
| Blood and lymphatic system disorders |                             |                    |                    |
| Anaemia                              |                             |                    |                    |
|                                      | subjects affected / exposed | 214 / 9539 (2.24%) | 240 / 9544 (2.51%) |
|                                      | occurrences (all)           | 221                | 249                |
| Eye disorders                        |                             |                    |                    |
| Cataract                             |                             |                    |                    |
|                                      | subjects affected / exposed | 157 / 9539 (1.65%) | 189 / 9544 (1.98%) |
|                                      | occurrences (all)           | 175                | 203                |
| Photopsia                            |                             |                    |                    |
|                                      | subjects affected / exposed | 509 / 9539 (5.34%) | 51 / 9544 (0.53%)  |
|                                      | occurrences (all)           | 567                | 52                 |
| Vision blurred                       |                             |                    |                    |
|                                      | subjects affected / exposed | 115 / 9539 (1.21%) | 36 / 9544 (0.38%)  |
|                                      | occurrences (all)           | 119                | 36                 |
| Gastrointestinal disorders           |                             |                    |                    |
| Constipation                         |                             |                    |                    |
|                                      | subjects affected / exposed | 99 / 9539 (1.04%)  | 102 / 9544 (1.07%) |
|                                      | occurrences (all)           | 106                | 107                |
| Diarrhoea                            |                             |                    |                    |
|                                      | subjects affected / exposed | 125 / 9539 (1.31%) | 121 / 9544 (1.27%) |
|                                      | occurrences (all)           | 131                | 129                |
| Gastritis                            |                             |                    |                    |
|                                      | subjects affected / exposed | 108 / 9539 (1.13%) | 124 / 9544 (1.30%) |
|                                      | occurrences (all)           | 111                | 127                |
| Nausea                               |                             |                    |                    |
|                                      | subjects affected / exposed | 96 / 9539 (1.01%)  | 83 / 9544 (0.87%)  |
|                                      | occurrences (all)           | 102                | 87                 |

|                                                 |                    |                    |  |
|-------------------------------------------------|--------------------|--------------------|--|
| Renal and urinary disorders                     |                    |                    |  |
| Renal failure                                   |                    |                    |  |
| subjects affected / exposed                     | 112 / 9539 (1.17%) | 89 / 9544 (0.93%)  |  |
| occurrences (all)                               | 118                | 90                 |  |
| Renal failure chronic                           |                    |                    |  |
| subjects affected / exposed                     | 105 / 9539 (1.10%) | 82 / 9544 (0.86%)  |  |
| occurrences (all)                               | 109                | 82                 |  |
| Musculoskeletal and connective tissue disorders |                    |                    |  |
| Back pain                                       |                    |                    |  |
| subjects affected / exposed                     | 102 / 9539 (1.07%) | 115 / 9544 (1.20%) |  |
| occurrences (all)                               | 107                | 121                |  |
| Arthralgia                                      |                    |                    |  |
| subjects affected / exposed                     | 71 / 9539 (0.74%)  | 98 / 9544 (1.03%)  |  |
| occurrences (all)                               | 75                 | 102                |  |
| Osteoarthritis                                  |                    |                    |  |
| subjects affected / exposed                     | 148 / 9539 (1.55%) | 192 / 9544 (2.01%) |  |
| occurrences (all)                               | 163                | 209                |  |
| Spinal osteoarthritis                           |                    |                    |  |
| subjects affected / exposed                     | 125 / 9539 (1.31%) | 134 / 9544 (1.40%) |  |
| occurrences (all)                               | 131                | 143                |  |
| Infections and infestations                     |                    |                    |  |
| Bronchitis                                      |                    |                    |  |
| subjects affected / exposed                     | 228 / 9539 (2.39%) | 201 / 9544 (2.11%) |  |
| occurrences (all)                               | 257                | 226                |  |
| Influenza                                       |                    |                    |  |
| subjects affected / exposed                     | 116 / 9539 (1.22%) | 169 / 9544 (1.77%) |  |
| occurrences (all)                               | 126                | 177                |  |
| Pneumonia                                       |                    |                    |  |
| subjects affected / exposed                     | 170 / 9539 (1.78%) | 146 / 9544 (1.53%) |  |
| occurrences (all)                               | 183                | 161                |  |
| Nasopharyngitis                                 |                    |                    |  |
| subjects affected / exposed                     | 172 / 9539 (1.80%) | 172 / 9544 (1.80%) |  |
| occurrences (all)                               | 195                | 198                |  |
| Upper respiratory tract infection               |                    |                    |  |
| subjects affected / exposed                     | 172 / 9539 (1.80%) | 179 / 9544 (1.88%) |  |
| occurrences (all)                               | 200                | 219                |  |

|                                                                                          |                           |                           |  |
|------------------------------------------------------------------------------------------|---------------------------|---------------------------|--|
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)              | 129 / 9539 (1.35%)<br>137 | 116 / 9544 (1.22%)<br>136 |  |
| Metabolism and nutrition disorders                                                       |                           |                           |  |
| Diabetes mellitus<br>subjects affected / exposed<br>occurrences (all)                    | 241 / 9539 (2.53%)<br>264 | 320 / 9544 (3.35%)<br>347 |  |
| Diabetes mellitus inadequate control<br>subjects affected / exposed<br>occurrences (all) | 109 / 9539 (1.14%)<br>115 | 132 / 9544 (1.38%)<br>141 |  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                       | 109 / 9539 (1.14%)<br>113 | 103 / 9544 (1.08%)<br>108 |  |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)                | 155 / 9539 (1.62%)<br>162 | 175 / 9544 (1.83%)<br>184 |  |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)                        | 152 / 9539 (1.59%)<br>159 | 121 / 9544 (1.27%)<br>131 |  |
| Type 2 diabetes mellitus<br>subjects affected / exposed<br>occurrences (all)             | 161 / 9539 (1.69%)<br>167 | 217 / 9544 (2.27%)<br>231 |  |
| Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all)                | 150 / 9539 (1.57%)<br>154 | 159 / 9544 (1.67%)<br>162 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 08 June 2010      | <p>Amendment No. 1 was applicable in all countries. The aims were:</p> <ul style="list-style-type: none"><li>- To update the list of secondary efficacy endpoints: a new endpoint "coronary death" (a sub-category of cardiovascular deaths) was added, based on the BEAUTIFUL data, where the benefits of ivabradine had been observed mainly on coronary events;</li><li>- To clarify the criteria for the documentation of the coronary artery disease (selection criteria). The e-CRF was modified to include more extensive details;</li><li>- To update the definition of an excessive intake of the study drug and the rules for immediate notification to the sponsor;</li><li>- To update administrative data (including the list of countries, the names and/or contact details of non-sponsor and sponsor parties), and to update the list of ancillary studies (Biomarkers of coronary artery disease ancillary study was added in selected centres).</li></ul> <p>The amendment did not require any changes to the patient information sheet or informed consent form.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 14 June 2011      | <p>Amendment No. 2, was applicable in all countries. The aims were:</p> <ul style="list-style-type: none"><li>- To increase the number of patients to be randomised (16 850 instead of 11 330 initially planned) and the extension of the estimated recruitment duration to 30 months (instead of 24 months). These changes were made on the basis of a revised annual incidence in blind for the primary composite endpoint of 2.5% in the overall population (corresponding to 2.7% in the placebo group), with unchanged power (90%), type I error (5%), and relative risk reduction (18%). The planned follow-up duration for the first included patients was extended from 42 months to 48 months.</li><li>- To update the administrative data (including the list of countries, the names and / or contact details of non-sponsor and sponsor parties).</li><li>- To clarify the types of source documents needed for the documentation of the CAD in the case of previous coronary revascularisation or presence of significant (&gt; 50%) coronary artery stenosis.</li><li>- To clarify that patient should receive stable doses of conventional CV medications during the run-in period.</li></ul> <p>This amendment required an amendment to the patient information and consent form. The amended form was to be signed by all patients as soon as the amendment became applicable in their centre: new patients were to sign the complete form, while patients already recruited in the study before the amendment were to sign the short form during their next visit after the amendment implementation.</p> |
| 07 September 2012 | <p>Amendment No. 4, was applicable in all countries. The aims were:</p> <ul style="list-style-type: none"><li>- To update information on concomitant treatments to be used with precaution during the study (potassium-depleting diuretics).</li><li>- To update the list of adverse events for which specific information was requested and already collected (bradycardia, eye disorders, rhythm and conduction disorders, blood pressure increases and QT prolongation).</li><li>- Additional clarifications and corrections, including definitions of the intensity of adverse events (mild, moderate, and severe).</li><li>- To update administrative data (Belarus and Saudi Arabia were removed from the list of participating countries).</li></ul> <p>This amendment required an amendment to the patient information and consent form.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

|             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 30 May 2013 | Amendment No. 5 and amendment No. 6 were applicable in all countries where it was permitted to retrieve, for patients who withdrew their study consent, their vital status (amendment No. 5) and the dates of hospitalisations for CV events (amendment No. 6). The aims of these amendments were to minimise the number of patients with missing follow-up information of vital status and hospitalisations for cardiovascular events at the end of the study, while respecting the local regulations. The patients concerned by this procedure were those who withdrew consent from study after the randomisation/inclusion visit and before the start date of the termination visits (scheduled from 1 September to 31 December 2013). In the cases where there was information that a PSE occurred, no PSE file was prepared and the event was not adjudicated by the EVC. Depending on local regulations, these two amendments may or may not have required an amendment to the patient information and consent form. |
|-------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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.

|                                                                                                                                                                                                                                                                   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>The section NSAE presented EAEs on treatment and included SEAEs. The causality and seriousness of reported SAE can be ultimately upgraded by the sponsor. The sponsor took these decisions to be compliant with the existing ICH E3 Clinical Study Report.</p> |
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Notes: