



## Clinical trial results:

### A Randomised, Controlled, Open-Label, Multicenter, Parallel-Group Study to Assess All-Cause Mortality and Cardiovascular Morbidity in Patients with Chronic Kidney Disease on Dialysis and Those Not on Renal Replacement Therapy under Treatment with MIRCERA® or Reference ESAs

#### Summary

|                          |                            |
|--------------------------|----------------------------|
| EudraCT number           | 2007-005129-31             |
| Trial protocol           | DE GB BE CZ IT SE LT GR FR |
| Global end of trial date | 27 July 2017               |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 03 August 2018 |
| First version publication date | 03 August 2018 |

#### Trial information

##### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | BH21260 |
|-----------------------|---------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00773513 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | F. Hoffmann-La Roche AG   |
| Sponsor organisation address | F. Hoffmann-La Roche AG, Basel, Switzerland, CH-4070  |
| Public contact               | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact           | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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                       | 20 June 2018 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 27 July 2017 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to demonstrate non-inferiority of methoxy polyethylene glycol-epoetin beta (MIRCERA) versus reference erythropoiesis-stimulating agents (ESAs) in terms of a composite endpoint of all cause mortality and non-fatal cardiovascular events (myocardial infarction [MI], stroke).

Protection of trial subjects:

All subjects signed an informed consent form before participating in the study.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 12 December 2008 |
| 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 | Malaysia: 17           |
| Country: Number of subjects enrolled | Philippines: 15        |
| Country: Number of subjects enrolled | Taiwan: 43             |
| Country: Number of subjects enrolled | Korea, Republic of: 16 |
| Country: Number of subjects enrolled | Singapore: 44          |
| Country: Number of subjects enrolled | Thailand: 54           |
| Country: Number of subjects enrolled | Turkey: 60             |
| Country: Number of subjects enrolled | Israel: 64             |
| Country: Number of subjects enrolled | Australia: 148         |
| Country: Number of subjects enrolled | Belgium: 95            |
| Country: Number of subjects enrolled | Croatia: 135           |
| Country: Number of subjects enrolled | Czech Republic: 74     |
| Country: Number of subjects enrolled | France: 269            |
| Country: Number of subjects enrolled | Germany: 281           |
| Country: Number of subjects enrolled | United Kingdom: 257    |
| Country: Number of subjects enrolled | Greece: 85             |
| Country: Number of subjects enrolled | Italy: 412             |
| Country: Number of subjects enrolled | Lithuania: 34          |
| Country: Number of subjects enrolled | Poland: 173            |
| Country: Number of subjects enrolled | Russian Federation: 37 |

|                                      |               |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Serbia: 81    |
| Country: Number of subjects enrolled | Spain: 130    |
| Country: Number of subjects enrolled | Sweden: 18    |
| Country: Number of subjects enrolled | Argentina: 84 |
| Country: Number of subjects enrolled | Brazil: 155   |
| Country: Number of subjects enrolled | Mexico: 32    |
| Country: Number of subjects enrolled | Panama: 12    |
| Worldwide total number of subjects   | 2825          |
| EEA total number of subjects         | 1963          |

Notes:

| <b>Subjects enrolled per age group</b>    |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 1407 |
| From 65 to 84 years                       | 1334 |
| 85 years and over                         | 84   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The subject population consisted of adults ( $\geq 18$  years old) with symptomatic anemia associated with chronic kidney disease (renal anemia).

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Not blinded                    |

### Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Erythropoiesis Stimulating Agents |

Arm description:

Participants received reference ESA according to approved label. No biosimilar ESAs were accepted in the study. The approved reference ESA compounds in the study were darbepoetin alfa, epoetin alfa and epoetin beta.

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Active comparator                 |
| Investigational medicinal product name | Darbepoetin alfa                  |
| Investigational medicinal product code |                                   |
| Other name                             | Aranesp®, Nespo®, Aranest®        |
| Pharmaceutical forms                   | Injection                         |
| Routes of administration               | Subcutaneous use, Intravenous use |

Dosage and administration details:

Darbepoetin alfa was administered as per approved label.

|  |                                   |
|--|-----------------------------------|
| Investigational medicinal product name | Epoetin beta                      |
| Investigational medicinal product code |                                   |
| Other name                             | Neorecormon®, Recormon®           |
| Pharmaceutical forms                   | Injection                         |
| Routes of administration               | Intravenous use, Subcutaneous use |

Dosage and administration details:

Epoetin beta was administered as per approved label.

|  |                                   |
|--|-----------------------------------|
| Investigational medicinal product name | Epoetin alfa                      |
| Investigational medicinal product code |                                   |
| Other name                             | Eprex®, Epogen®, Epopen®, Erypo®  |
| Pharmaceutical forms                   | Injection                         |
| Routes of administration               | Intravenous use, Subcutaneous use |

Dosage and administration details:

Epoetin alfa was administered as per approved label.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Methoxy Polyethylene Glycol-Epoetin Beta |
|------------------|--|

Arm description:

Subjects not currently being treated with an ESA received 0.6 micrograms per kilogram (mcg/kg) methoxy polyethylene glycol-epoetin beta intravenously (iv) or subcutaneously (sc) once every 2 weeks for correction of renal anemia (target hemoglobin [Hb] 10-12 grams per deciliter [g/dL]). Subjects currently treated with an ESA received a starting dose of 120, 200 or 360 mcg/kg methoxy polyethylene glycol-epoetin beta iv or sc once monthly based on the calculated weekly ESA dose prior to the switch for maintenance of anemia treatment. Once corrected and in subjects currently being treated with an ESA, methoxy polyethylene glycol-epoetin beta was administered once monthly.

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | Darbepoetin alfa                  |
| Investigational medicinal product code |                                   |
| Other name                             | Aranesp®, Nespo®, Aranest®        |
| Pharmaceutical forms                   | Injection                         |
| Routes of administration               | Intravenous use, Subcutaneous use |

Dosage and administration details:

Darbepoetin alfa was administered as per approved label.

|  |                                   |
|--|-----------------------------------|
| Investigational medicinal product name | Epoetin alfa                      |
| Investigational medicinal product code |                                   |
| Other name                             | Eprex®, Epogen®, Epopen®, Erypo®  |
| Pharmaceutical forms                   | Injection                         |
| Routes of administration               | Intravenous use, Subcutaneous use |

Dosage and administration details:

Epoetin alfa was administered as per approved label.

|  |  |
|--|--|
| Investigational medicinal product name | Methoxy polyethylene glycol-epoetin beta |
| Investigational medicinal product code |  |
| Other name                             | Mircera®                                 |
| Pharmaceutical forms                   | Injection                                |
| Routes of administration               | Intravenous use, Subcutaneous use        |

Dosage and administration details:

Subjects who were currently not being treated with an ESA received methoxy polyethylene glycol-epoetin beta administered at a starting dose of 0.6 mcg/kg body weight once every 2 weeks. Subjects who were currently being treated with an ESA received methoxy polyethylene glycol-epoetin beta at a dose of 120, 200 or 360 mcg once monthly (based on ESA dose administered in Week -1).

| Number of subjects in period 1        | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |
|---------------------------------------|-----------------------------------|--|
|                                       |                                   |  |
| Started                               | 1413                              | 1412                                     |
| Completed                             | 312                               | 303                                      |
| Not completed                         | 1101                              | 1109                                     |
| Withdrew Consent                      | 68                                | 69                                       |
| Renal Transplant                      | 254                               | 263                                      |
| Reason Not Specified                  | 159                               | 126                                      |
| Death                                 | 531                               | 545                                      |
| Adverse Event / Intercurrent Illness  | 40                                | 48                                       |
| Failure to Return                     | 22                                | 8  |
| Insufficient Therapeutic Response     | 1                                 | 18                                       |
| Refused Treatment / Did Not Cooperate | 26                                | 32                                       |

## Baseline characteristics

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Erythropoiesis Stimulating Agents |
|-----------------------|-----------------------------------|

Reporting group description:

Participants received reference ESA according to approved label. No biosimilar ESAs were accepted in the study. The approved reference ESA compounds in the study were darbepoetin alfa, epoetin alfa and epoetin beta.

|                       |  |
|-----------------------|--|
| Reporting group title | Methoxy Polyethylene Glycol-Epoetin Beta |
|-----------------------|--|

Reporting group description:

Subjects not currently being treated with an ESA received 0.6 micrograms per kilogram (mcg/kg) methoxy polyethylene glycol-epoetin beta intravenously (iv) or subcutaneously (sc) once every 2 weeks for correction of renal anemia (target hemoglobin [Hb] 10-12 grams per deciliter [g/dL]). Subjects currently treated with an ESA received a starting dose of 120, 200 or 360 mcg/kg methoxy polyethylene glycol-epoetin beta iv or sc once monthly based on the calculated weekly ESA dose prior to the switch for maintenance of anemia treatment. Once corrected and in subjects currently being treated with an ESA, methoxy polyethylene glycol-epoetin beta was administered once monthly.

| Reporting group values             | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta | Total |
|------------------------------------|-----------------------------------|--|-------|
| Number of subjects                 | 1413                              | 1412                                     | 2825  |
| Age categorical<br>Units: Subjects |                                   |  |       |

|   |                |                |      |
|---|----------------|----------------|------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 62.6<br>± 14.8 | 62.2<br>± 15.0 | -    |
| Gender categorical<br>Units: Subjects                                   |                |                |      |
| Female  | 581            | 605            | 1186 |
| Male  | 832            | 807            | 1639 |
| Race/Ethnicity, Customized<br>Units: Subjects                           |                |                |      |
| White   | 1221           | 1218           | 2439 |
| Asian   | 111            | 119            | 230  |
| Black or African American   | 40             | 37             | 77   |
| Other   | 41             | 38             | 79   |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Erythropoiesis Stimulating Agents        |
| Reporting group description:<br>Participants received reference ESA according to approved label. No biosimilar ESAs were accepted in the study. The approved reference ESA compounds in the study were darbepoetin alfa, epoetin alfa and epoetin beta.  |  |
| Reporting group title  | Methoxy Polyethylene Glycol-Epoetin Beta |
| Reporting group description:<br>Subjects not currently being treated with an ESA received 0.6 micrograms per kilogram (mcg/kg) methoxy polyethylene glycol-epoetin beta intravenously (iv) or subcutaneously (sc) once every 2 weeks for correction of renal anemia (target hemoglobin [Hb] 10-12 grams per deciliter [g/dL]). Subjects currently treated with an ESA received a starting dose of 120, 200 or 360 mcg/kg methoxy polyethylene glycol-epoetin beta iv or sc once monthly based on the calculated weekly ESA dose prior to the switch for maintenance of anemia treatment. Once corrected and in subjects currently being treated with an ESA, methoxy polyethylene glycol-epoetin beta was administered once monthly. |  |

### **Primary: Time to Composite of All-Cause Mortality and Non-Fatal Cardiovascular Events (Myocardial Infarction, Stroke) Defined as Time Between First Dose of Study Medication and Date of Death or Non-Fatal Cardiovascular Events, Whichever Occurred First**

|  |  |
|--|--|
| End point title  | Time to Composite of All-Cause Mortality and Non-Fatal Cardiovascular Events (Myocardial Infarction, Stroke) Defined as Time Between First Dose of Study Medication and Date of Death or Non-Fatal Cardiovascular Events, Whichever Occurred First |
| End point description:<br>The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose safety assessment. Data are reported for subjects with an event. |  |
| End point type   | Primary  |
| End point timeframe:<br>Baseline up to approximately 8.5 years   |  |

| End point values                 | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| Subject group type               | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed      | 1409                              | 1409                                     |  |  |
| Units: years                     |                                   |  |  |  |
| median (confidence interval 95%) | 5.1 (4.8 to 5.6)                  | 5.1 (4.7 to 5.4)                         |  |  |

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Statistical Analysis 1   |
| Comparison groups          | Erythropoiesis Stimulating Agents v Methoxy Polyethylene Glycol-Epoetin Beta |

|   |                                |
|---|--------------------------------|
| Number of subjects included in analysis | 2818                           |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[1]</sup> |
| P-value                                 | = 0.0039                       |
| Method                                  | Regression, Cox                |
| Parameter estimate                      | Hazard ratio (HR)              |
| Point estimate                          | 1.03                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | 0.93                           |
| upper limit                             | 1.15                           |

Notes:

[1] - The critical alpha level for the non-inferiority test was 0.025. The pre-specified upper non-inferiority limit was 95% CI <1.20.

## Secondary: Time to All-Cause Mortality

|  |                             |
|--|-----------------------------|
| End point title  | Time to All-Cause Mortality |
| End point description:   |                             |
| The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose safety assessment. Data are reported for subjects with an event. |                             |
| End point type   | Secondary                   |
| End point timeframe:   |                             |
| Baseline up to approximately 8.5 years   |                             |

| End point values                 | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| Subject group type               | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed      | 1409                              | 1409                                     |  |  |
| Units: years                     |                                   |  |  |  |
| median (confidence interval 95%) | 6.1 (5.6 to 6.5)                  | 5.9 (5.5 to 6.5)                         |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 2   |
| Comparison groups                       | Erythropoiesis Stimulating Agents v Methoxy Polyethylene Glycol-Epoetin Beta |
| Number of subjects included in analysis | 2818   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority  |
| P-value                                 | = 0.0166   |
| Method                                  | Regression, Cox  |
| Parameter estimate                      | Hazard ratio (HR)  |
| Point estimate                          | 1.06   |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.94    |
| upper limit         | 1.19    |

## Secondary: Time to Non-Fatal and Fatal Myocardial Infarction

|  |   |
|--|---|
| End point title  | Time to Non-Fatal and Fatal Myocardial Infarction |
| End point description:   |   |
| The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose safety assessment. Analysis was performed on data for subjects with an event. 9999 = median time to event was not reached. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline up to approximately 8.5 years   |   |

| End point values                 | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| Subject group type               | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed      | 1409                              | 1409                                     |  |  |
| Units: years                     |                                   |  |  |  |
| median (confidence interval 95%) | 9999 (9999 to 9999)               | 9999 (9999 to 9999)                      |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Statistical Analysis 3   |
| Comparison groups                       | Erythropoiesis Stimulating Agents v Methoxy Polyethylene Glycol-Epoetin Beta |
| Number of subjects included in analysis | 2818   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority  |
| P-value                                 | = 0.0219   |
| Method                                  | Regression, Cox  |
| Parameter estimate                      | Hazard ratio (HR)  |
| Point estimate                          | 0.95   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.76   |
| upper limit                             | 1.19   |

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**Secondary: Time to Non-Fatal and Fatal Stroke**

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|                 |                                    |
|-----------------|------------------------------------|
| End point title | Time to Non-Fatal and Fatal Stroke |
|-----------------|------------------------------------|

End point description:

The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose safety assessment. Analysis was performed on data for subjects with an event. 9999 = median time to event was not reached.

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

End point timeframe:

Baseline up to approximately 8.5 years

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| End point values                 | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| Subject group type               | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed      | 1409                              | 1409                                     |  |  |
| Units: years                     |                                   |  |  |  |
| median (confidence interval 95%) | 9999 (9999 to 9999)               | 9999 (9999 to 9999)                      |  |  |

**Statistical analyses**

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Statistical Analysis 4   |
| Comparison groups                       | Erythropoiesis Stimulating Agents v Methoxy Polyethylene Glycol-Epoetin Beta |
| Number of subjects included in analysis | 2818   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority  |
| P-value                                 | = 0.0459   |
| Method                                  | Regression, Cox  |
| Parameter estimate                      | Hazard ratio (HR)  |
| Point estimate                          | 0.94   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.7  |
| upper limit                             | 1.25   |

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**Secondary: Time to Non-Fatal Cardiovascular Events (Myocardial Infarction or Stroke, Whichever Occurred First)**

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|                 |   |
|-----------------|---|
| End point title | Time to Non-Fatal Cardiovascular Events (Myocardial Infarction or Stroke, Whichever Occurred First) |
|-----------------|---|

End point description:

The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose safety assessment. Analysis was performed on data for subjects with an event. 9999 = median time to event was not reached.

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

End point timeframe:

Baseline up to approximately 8.5 years

| End point values                 | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| Subject group type               | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed      | 1409                              | 1409                                     |  |  |
| Units: years                     |                                   |  |  |  |
| median (confidence interval 95%) | 9999 (9999 to 9999)               | 9999 (9999 to 9999)                      |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Statistical Analysis 5   |
| Comparison groups                       | Erythropoiesis Stimulating Agents v Methoxy Polyethylene Glycol-Epoetin Beta |
| Number of subjects included in analysis | 2818   |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | non-inferiority  |
| P-value                                 | = 0.0048   |
| Method                                  | Regression, Cox  |
| Parameter estimate                      | Hazard ratio (HR)  |
| Point estimate                          | 0.91   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.74   |
| upper limit                             | 1.12   |

## Secondary: Percentage of Subjects With Anti-Erythropoietin Antibody-Mediated Pure Red Cell Aplasia (PRCA)

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Anti-Erythropoietin Antibody-Mediated Pure Red Cell Aplasia (PRCA) |
|-----------------|--|

End point description:

The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose safety assessment.

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

End point timeframe:

Baseline up to approximately 8.5 years

| End point values              | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|-------------------------------|-----------------------------------|--|--|--|
| Subject group type            | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed   | 1409                              | 1409                                     |  |  |
| Units: percentage of subjects |                                   |  |  |  |
| number (not applicable)       | 0                                 | 0  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Gastrointestinal Bleeding

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Gastrointestinal Bleeding |
|-----------------|---|

End point description:

The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose safety assessment.

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

End point timeframe:

Baseline up to approximately 8.5 years

| End point values              | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|-------------------------------|-----------------------------------|--|--|--|
| Subject group type            | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed   | 1409                              | 1409                                     |  |  |
| Units: percentage of subjects |                                   |  |  |  |
| number (not applicable)       | 11.1                              | 11.7                                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Thromboembolic Events

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Thromboembolic Events |
|-----------------|---|

End point description:

The safety population included all subjects randomised (with the appropriate signed consent documentation), who received at least one dose of the trial medication and had at least one post-dose

safety assessment.

|  |           |
|--|-----------|
| End point type                         | Secondary |
| End point timeframe:                   |           |
| Baseline up to approximately 8.5 years |           |

| End point values              | Erythropoiesis Stimulating Agents | Methoxy Polyethylene Glycol-Epoetin Beta |  |  |
|-------------------------------|-----------------------------------|--|--|--|
| Subject group type            | Reporting group                   | Reporting group                          |  |  |
| Number of subjects analysed   | 1409                              | 1409                                     |  |  |
| Units: percentage of subjects |                                   |  |  |  |
| number (not applicable)       | 34.5                              | 32.8                                     |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to approximately 8.5 years.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Methoxy Polyethylene Glycol-Epoetin Beta |
|-----------------------|--|

Reporting group description:

Subjects not currently being treated with an ESA received 0.6 micrograms per kilogram (mcg/kg) methoxy polyethylene glycol-epoetin beta intravenously (iv) or subcutaneously (sc) once every 2 weeks for correction of renal anemia (target hemoglobin [Hb] 10-12 grams per deciliter [g/dL]). Subjects currently treated with an ESA received a starting dose of 120, 200 or 360 mcg/kg methoxy polyethylene glycol-epoetin beta iv or sc once monthly based on the calculated weekly ESA dose prior to the switch for maintenance of anemia treatment. Once corrected and in subjects currently being treated with an ESA, methoxy polyethylene glycol-epoetin beta was administered once monthly.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Erythropoiesis Stimulating Agents |
|-----------------------|-----------------------------------|

Reporting group description:

Participants received reference ESA according to approved label. No biosimilar ESAs were accepted in the study. The approved reference ESA compounds in the study were darbepoetin alfa, epoetin alfa and epoetin beta.

| Serious adverse events  | Methoxy Polyethylene Glycol-Epoetin Beta | Erythropoiesis Stimulating Agents |  |
|---|--|-----------------------------------|--|
| Total subjects affected by serious adverse events                   |  |                                   |  |
| subjects affected / exposed   | 1097 / 1409 (77.86%)                     | 1123 / 1409 (79.70%)              |  |
| number of deaths (all causes)                                       | 558                                      | 557                               |  |
| number of deaths resulting from adverse events                      |  |                                   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |                                   |  |
| Basal cell carcinoma  |  |                                   |  |
| subjects affected / exposed   | 8 / 1409 (0.57%)                         | 6 / 1409 (0.43%)                  |  |
| occurrences causally related to treatment / all                     | 0 / 8                                    | 0 / 6                             |  |
| deaths causally related to treatment / all                          | 0 / 0                                    | 0 / 0                             |  |
| Breast cancer   |  |                                   |  |
| subjects affected / exposed   | 6 / 1409 (0.43%)                         | 3 / 1409 (0.21%)                  |  |
| occurrences causally related to treatment / all                     | 0 / 6                                    | 0 / 3                             |  |
| deaths causally related to treatment / all                          | 0 / 0                                    | 0 / 0                             |  |
| Squamous cell carcinoma   |  |                                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostate cancer                                 |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to liver                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |
| Renal cell carcinoma                            |                  |                  |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder neoplasm                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Colon cancer metastatic                         |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 1            |  |
| Myelodysplastic syndrome                        |                  |                  |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 6            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cancer                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Squamous cell carcinoma of skin                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adenocarcinoma of colon                         |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder transitional cell carcinoma             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon adenoma                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostate cancer metastatic                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Rectal cancer                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Cholangiocarcinoma                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 3            |  |
| Intestinal adenocarcinoma                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Renal cancer metastatic                         |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Skin cancer                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| B-cell lymphoma                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Colon cancer                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal tract adenoma                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung neoplasm                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Lung neoplasm malignant                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Malignant melanoma                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant pleural effusion                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastases to central nervous system            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Metastases to lung                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Pancreatic carcinoma                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Pituitary tumour benign                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma of lung                 |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Transitional cell carcinoma                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Bladder papilloma                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone neoplasm                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchial carcinoma                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Colorectal cancer                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Gastric cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cancer                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cancer metastatic                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hepatocellular carcinoma                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Lung adenocarcinoma                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastases to bone                              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastatic carcinoma of the bladder             |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Metastatic malignant melanoma                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastatic neoplasm                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Neuroendocrine tumour                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal carcinoma                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatic neoplasm                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Papillary thyroid cancer                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Plasma cell myeloma                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostate cancer recurrent                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Rectal adenocarcinoma                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Squamous cell carcinoma of the tongue           |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroid adenoma                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroid cancer metastatic                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute myeloid leukaemia                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Acute myelomonocytic leukaemia                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Adenoma benign                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adrenal adenoma                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign lung neoplasm                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign neoplasm of bladder                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign neoplasm of epididymis                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Benign urinary tract neoplasm                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder cancer recurrent                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder transitional cell carcinoma metastatic  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Brain neoplasm                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain neoplasm malignant                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carcinoid tumour of the duodenum                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Carcinoma in situ of penis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Central nervous system lymphoma                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Central nervous system neoplasm                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral hygroma                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervix cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervix carcinoma                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Choroid melanoma                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic myeloid leukaemia                       |                  |                  |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                          | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Colorectal adenocarcinoma                            |                  |                  |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Connective tissue neoplasm                           |                  |                  |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 1            |  |
| Ear neoplasm malignant                               |                  |                  |  |
| subjects affected / exposed                          | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Endometrial cancer                                   |                  |                  |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Endometrial neoplasm                                 |                  |                  |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 1            |  |
| Extranodal marginal zone B-cell lymphoma (malt type) |                  |                  |  |
| subjects affected / exposed                          | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all           | 0 / 0            | 0 / 0            |  |
| Gallbladder adenocarcinoma                           |                  |                  |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Glioma</b>                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Hepatic neoplasm</b>                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| <b>Invasive ductal breast carcinoma</b>         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Invasive lobular breast carcinoma</b>        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Keratoacanthoma</b>                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Laryngeal papilloma</b>                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Lentigo maligna</b>                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Lung cancer metastatic</b>                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lung squamous cell carcinoma metastatic         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malignant fibrous histiocytoma                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastases to peritoneum                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastases to spine                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Metastatic carcinoid tumour                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastatic gastric cancer                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Metastatic renal cell carcinoma                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metastatic squamous cell carcinoma              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myelofibrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neoplasm skin                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuroendocrine carcinoma metastatic             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Non-Hodgkin's lymphoma                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Oesophageal adenocarcinoma                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Oligodendroglioma                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian adenoma                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paget's disease of nipple                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatic carcinoma metastatic                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Parathyroid tumour benign                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic neoplasm                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Plasma cell myeloma recurrent                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal cancer metastatic                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Rectal cancer recurrent                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectosigmoid cancer                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Refractory cytopenia with unilineage dysplasia  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 recurrent                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal haemangioma                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small cell lung cancer metastatic               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 oral cavity      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Testicular neoplasm                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thymoma   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thyroid cancer                                  |                  |                  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                                    | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all                | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                     | 0 / 0            | 0 / 0            |  |
| Tongue neoplasm malignant stage unspecified                    |                  |                  |  |
| subjects affected / exposed                                    | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                     | 0 / 0            | 0 / 1            |  |
| Tonsil cancer  |                  |                  |  |
| subjects affected / exposed                                    | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                     | 0 / 0            | 0 / 1            |  |
| Transitional cell cancer of renal pelvis and ureter metastatic |                  |                  |  |
| subjects affected / exposed                                    | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                     | 0 / 0            | 0 / 1            |  |
| Transitional cell carcinoma urethra                            |                  |                  |  |
| subjects affected / exposed                                    | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                     | 0 / 0            | 0 / 1            |  |
| Tumour haemorrhage   |                  |                  |  |
| subjects affected / exposed                                    | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all                | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all                     | 0 / 0            | 0 / 0            |  |
| Urinary bladder adenoma  |                  |                  |  |
| subjects affected / exposed                                    | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                                    | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                     | 0 / 0            | 0 / 0            |  |
| Vascular disorders   |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| Peripheral ischaemia                            |                   |                   |  |
| subjects affected / exposed                     | 31 / 1409 (2.20%) | 31 / 1409 (2.20%) |  |
| occurrences causally related to treatment / all | 1 / 39            | 0 / 36            |  |
| deaths causally related to treatment / all      | 0 / 4             | 0 / 5             |  |
| Peripheral arterial occlusive disease           |                   |                   |  |
| subjects affected / exposed                     | 24 / 1409 (1.70%) | 24 / 1409 (1.70%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Hypertension                                    |                   |                   |  |
| subjects affected / exposed                     | 23 / 1409 (1.63%) | 24 / 1409 (1.70%) |  |
| occurrences causally related to treatment / all | 1 / 33            | 2 / 27            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypotension                                     |                   |                   |  |
| subjects affected / exposed                     | 16 / 1409 (1.14%) | 18 / 1409 (1.28%) |  |
| occurrences causally related to treatment / all | 1 / 16            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Extremity necrosis                              |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 13 / 1409 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Hypertensive crisis                             |                   |                   |  |
| subjects affected / exposed                     | 13 / 1409 (0.92%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Peripheral artery stenosis                      |                   |                   |  |
| subjects affected / exposed                     | 12 / 1409 (0.85%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Peripheral vascular disorder                    |                   |                   |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%)  | 11 / 1409 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Aortic stenosis                                 |                   |                   |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 11 / 1409 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Deep vein thrombosis                            |                  |                   |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%) | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 1 / 7            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Orthostatic hypotension                         |                  |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Haematoma                                       |                  |                   |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%) | 5 / 1409 (0.35%)  |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| Shock haemorrhagic                              |                  |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 6 / 1409 (0.43%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 3             |  |
| Aortic aneurysm                                 |                  |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 5 / 1409 (0.35%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1             |  |
| Steal syndrome                                  |                  |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 2 / 1409 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Dry gangrene                                    |                  |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Intermittent claudication                       |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral artery occlusion                     |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Venous stenosis                                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Circulatory collapse                            |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 3            |  |
| Aortic aneurysm rupture                         |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 4            | 0 / 1            |  |
| Brachiocephalic vein stenosis                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral artery thrombosis                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Angiopathy                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial disorder                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Granulomatosis with polyangiitis                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypovolaemic shock                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Vena cava thrombosis                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous thrombosis limb                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial occlusive disease                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Shock   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Superior vena cava syndrome                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombosis                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Angiodysplasia                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic dissection                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial haemorrhage                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial rupture                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriosclerosis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brachiocephalic vein thrombosis                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic macroangiopathy                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic vascular disorder                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhage                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertensive emergency                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leriche syndrome                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral embolism                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Phlebitis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subclavian vein stenosis                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombophlebitis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular calcification                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Venous thrombosis                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aneurysm  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic arteriosclerosis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic thrombosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic infarction                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Ischaemia                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic limb pain                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphatic fistula                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymphoedema                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Microangiopathy                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Microscopic polyangiitis                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic venous thrombosis                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral artery aneurysm                      |                  |                  |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| subjects affected / exposed                          | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0             |  |
| Varicose vein  |                   |                   |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0             |  |
| Vascular stenosis                                    |                   |                   |  |
| subjects affected / exposed                          | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0             |  |
| Vasculitis   |                   |                   |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0             |  |
| Vasculitis necrotising                               |                   |                   |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0             |  |
| Venous aneurysm                                      |                   |                   |  |
| subjects affected / exposed                          | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0             |  |
| Surgical and medical procedures                      |                   |                   |  |
| Oral surgery   |                   |                   |  |
| subjects affected / exposed                          | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all           | 0 / 0             | 0 / 0             |  |
| General disorders and administration site conditions |                   |                   |  |
| Death  |                   |                   |  |
| subjects affected / exposed                          | 39 / 1409 (2.77%) | 33 / 1409 (2.34%) |  |
| occurrences causally related to treatment / all      | 0 / 39            | 0 / 33            |  |
| deaths causally related to treatment / all           | 0 / 39            | 0 / 33            |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| Sudden death                                    |                   |                   |  |
| subjects affected / exposed                     | 44 / 1409 (3.12%) | 26 / 1409 (1.85%) |  |
| occurrences causally related to treatment / all | 0 / 44            | 0 / 26            |  |
| deaths causally related to treatment / all      | 0 / 44            | 0 / 26            |  |
| Pyrexia   |                   |                   |  |
| subjects affected / exposed                     | 26 / 1409 (1.85%) | 30 / 1409 (2.13%) |  |
| occurrences causally related to treatment / all | 0 / 31            | 0 / 39            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| General physical health deterioration           |                   |                   |  |
| subjects affected / exposed                     | 12 / 1409 (0.85%) | 16 / 1409 (1.14%) |  |
| occurrences causally related to treatment / all | 0 / 17            | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 6             | 0 / 11            |  |
| Chest pain                                      |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 13 / 1409 (0.92%) |  |
| occurrences causally related to treatment / all | 1 / 10            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Catheter site haemorrhage                       |                   |                   |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Non-cardiac chest pain                          |                   |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 11 / 1409 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Asthenia  |                   |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Inflammation                                    |                   |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Multiple organ dysfunction syndrome             |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 6            |  |
| Complication associated with device             |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sudden cardiac death                            |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 3            | 0 / 4            |  |
| Hyperthermia                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Adverse drug reaction                           |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device related thrombosis                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperpyrexia                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Malaise   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oedema due to renal disease                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fatigue   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hernia  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oedema peripheral                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Swelling  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Catheter site inflammation                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chest discomfort                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gait disturbance                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oedema  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Strangulated hernia                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Systemic inflammatory response syndrome         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Accidental death                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Discomfort                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Drug intolerance                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dysplasia                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Heteroplasia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Impaired healing                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Implant site extravasation                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incarcerated hernia                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injection site extravasation                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injection site scab                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Medical device pain                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mucosal ulceration                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Necrosis  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oedema due to cardiac disease                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pseudocyst                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stent-graft endoleak                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Surgical failure                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Treatment failure                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular stent restenosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular stent stenosis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular stent thrombosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Vessel puncture site haematoma                  |                  |                  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                              | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Immune system disorders                                  |                  |                  |  |
| Drug hypersensitivity                                    |                  |                  |  |
| subjects affected / exposed                              | 2 / 1409 (0.14%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all          | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Hypersensitivity   |                  |                  |  |
| subjects affected / exposed                              | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all          | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Kidney transplant rejection                              |                  |                  |  |
| subjects affected / exposed                              | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all          | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Anti-neutrophil cytoplasmic antibody positive vasculitis |                  |                  |  |
| subjects affected / exposed                              | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all          | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Anaphylactic shock                                       |                  |                  |  |
| subjects affected / exposed                              | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all          | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Graft versus host disease                                |                  |                  |  |
| subjects affected / exposed                              | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Immune reconstitution inflammatory syndrome              |                  |                  |  |
| subjects affected / exposed                              | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all          | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all               | 0 / 0            | 0 / 0            |  |
| Pancreas transplant rejection                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sarcoidosis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Transplant rejection                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Reproductive system and breast disorders        |                  |                  |  |
| Benign prostatic hyperplasia                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Prostatitis                                     |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endometrial hyperplasia                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervical dysplasia                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic ovarian cyst                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ovarian cyst                                    |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postmenopausal haemorrhage                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| 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                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Breast mass                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Hysterocele                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Menorrhagia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metrorrhagia                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Uterine polyp                                   |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (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 |                   |                   |  |
| Pleural effusion                                |                   |                   |  |
| subjects affected / exposed                     | 22 / 1409 (1.56%) | 22 / 1409 (1.56%) |  |
| occurrences causally related to treatment / all | 0 / 23            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Non-cardiogenic pulmonary oedema                |                   |                   |  |
| subjects affected / exposed                     | 15 / 1409 (1.06%) | 23 / 1409 (1.63%) |  |
| occurrences causally related to treatment / all | 0 / 18            | 0 / 35            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 3             |  |
| Dyspnoea  |                   |                   |  |
| subjects affected / exposed                     | 16 / 1409 (1.14%) | 14 / 1409 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 17            | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Pulmonary oedema                                |                   |                   |  |
| subjects affected / exposed                     | 18 / 1409 (1.28%) | 12 / 1409 (0.85%) |  |
| occurrences causally related to treatment / all | 1 / 19            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 4             | 0 / 2             |  |
| Acute pulmonary oedema                          |                   |                   |  |
| subjects affected / exposed                     | 11 / 1409 (0.78%) | 14 / 1409 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 4             |  |
| Chronic obstructive pulmonary disease           |                   |                   |  |
| subjects affected / exposed                     | 12 / 1409 (0.85%) | 11 / 1409 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |  |
| Respiratory failure                             |                   |                   |  |
| subjects affected / exposed                     | 13 / 1409 (0.92%) | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 13            | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 9             | 0 / 3             |  |
| Pneumonia aspiration                            |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 9 / 1409 (0.64%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 3            |  |
| Epistaxis                                       |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 8 / 1409 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary embolism                              |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 9 / 1409 (0.64%) |  |
| occurrences causally related to treatment / all | 1 / 5            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 3            |  |
| Acute respiratory failure                       |                  |                  |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 3            |  |
| Pulmonary congestion                            |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Lung disorder                                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonitis                                     |                  |                  |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Haemothorax                                     |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aspiration                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |
| Respiratory arrest                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Asthma  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Respiratory distress                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Bronchitis chronic                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchospasm                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemoptysis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary hypertension                          |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sleep apnoea syndrome                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchial disorder                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchiectasis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dyspnoea exertional                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydrothorax                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Interstitial lung disease                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasal polyps                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pleurisy  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumothorax                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Pulmonary mass                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute lung injury                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute respiratory distress syndrome             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Atelectasis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchopneumopathy                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cough   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hiccups   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Idiopathic pulmonary fibrosis                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mediastinal effusion                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mendelson's syndrome                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Nasal septum perforation                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Painful respiration                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary alveolar haemorrhage                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary arterial hypertension                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pulmonary thrombosis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Respiratory depression                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Psychiatric disorders                           |                   |                   |  |
| Confusional state                               |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 14 / 1409 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Completed suicide                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 3             |  |
| Delirium  |                   |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hallucination                                   |                   |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Depression                                      |                   |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 2 / 1409 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Sopor   |                   |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Adjustment disorder                             |                   |                   |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mania   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mental status changes                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Organic brain syndrome                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Suicide attempt                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abnormal behaviour                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute psychosis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anxiety   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anxiety disorder                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bipolar disorder                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Drug abuse                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mental disorder                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psychotic disorder                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Substance-induced psychotic disorder            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Product issues                                  |                  |                  |  |
| Device malfunction                              |                  |                  |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 7 / 1409 (0.50%) |  |
| occurrences causally related to treatment / all | 1 / 9            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombosis in device                            |                  |                  |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 13           | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device dislocation                              |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device loosening                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device breakage                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device damage                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device extrusion                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Device failure                                  |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| 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                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hepatobiliary disorders                         |                   |                   |  |
| Cholecystitis                                   |                   |                   |  |
| subjects affected / exposed                     | 12 / 1409 (0.85%) | 10 / 1409 (0.71%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cholecystitis acute                             |                   |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 1409 (0.50%) | 13 / 1409 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Cholelithiasis                                  |                  |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Cholangitis                                     |                  |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 5 / 1409 (0.35%)  |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Jaundice cholestatic                            |                  |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| Bile duct stone                                 |                  |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hepatic failure                                 |                  |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1             |  |
| Cholestasis                                     |                  |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Hepatic cirrhosis                               |                  |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Biliary colic                                   |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholangitis acute                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Drug-induced liver injury                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute hepatic failure                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Bile duct obstruction                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholecystitis chronic                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cirrhosis alcoholic                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gallbladder enlargement                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gallbladder perforation                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemobilia                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic artery stenosis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hepatitis acute                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatotoxicity                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydrocholecystis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Liver disorder                                  |                  |                  |  |

|   |                   |                    |  |
|---|-------------------|--------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)   |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Liver injury                                    |                   |                    |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)   |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Investigations                                  |                   |                    |  |
| Weight decreased                                |                   |                    |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 1 / 1409 (0.07%)   |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| International normalised ratio increased        |                   |                    |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 0 / 1409 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Coagulation time prolonged                      |                   |                    |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Investigation abnormal                          |                   |                    |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)   |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Troponin increased                              |                   |                    |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| Injury, poisoning and procedural complications  |                   |                    |  |
| Arteriovenous fistula thrombosis                |                   |                    |  |
| subjects affected / exposed                     | 77 / 1409 (5.46%) | 110 / 1409 (7.81%) |  |
| occurrences causally related to treatment / all | 2 / 106           | 4 / 141            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| Arteriovenous fistula site complication         |                   |                   |  |
| subjects affected / exposed                     | 47 / 1409 (3.34%) | 57 / 1409 (4.05%) |  |
| occurrences causally related to treatment / all | 0 / 65            | 0 / 69            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Femur fracture                                  |                   |                   |  |
| subjects affected / exposed                     | 26 / 1409 (1.85%) | 23 / 1409 (1.63%) |  |
| occurrences causally related to treatment / all | 0 / 27            | 0 / 24            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Arteriovenous fistula site haemorrhage          |                   |                   |  |
| subjects affected / exposed                     | 23 / 1409 (1.63%) | 16 / 1409 (1.14%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 1 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriovenous graft thrombosis                  |                   |                   |  |
| subjects affected / exposed                     | 23 / 1409 (1.63%) | 13 / 1409 (0.92%) |  |
| occurrences causally related to treatment / all | 1 / 44            | 1 / 39            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Femoral neck fracture                           |                   |                   |  |
| subjects affected / exposed                     | 14 / 1409 (0.99%) | 19 / 1409 (1.35%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Procedural hypotension                          |                   |                   |  |
| subjects affected / exposed                     | 16 / 1409 (1.14%) | 13 / 1409 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 17            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arteriovenous fistula aneurysm                  |                   |                   |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%)  | 15 / 1409 (1.06%) |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Subdural haematoma                              |                   |                   |  |
| subjects affected / exposed                     | 12 / 1409 (0.85%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 12            | 1 / 8             |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 2             |  |
| Hip fracture                                    |                   |                   |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 11 / 1409 (0.78%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Post procedural haemorrhage                     |                   |                   |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%)  | 11 / 1409 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |  |
| Rib fracture                                    |                   |                   |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%)  | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Head injury                                     |                   |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Humerus fracture                                |                   |                   |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Fall  |                   |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Multiple fractures                              |                   |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%)  | 5 / 1409 (0.35%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Overdose  |                   |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 6 / 1409 (0.43%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Pelvic fracture                                 |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 8 / 1409 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar vertebral fracture                       |                  |                  |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Limb injury                                     |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radius fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subarachnoid haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ankle fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous graft site stenosis               |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lower limb fracture                             |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Spinal compression fracture                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 6 / 1409 (0.43%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous fistula site haematoma            |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Contusion                                       |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural haematoma                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pubis fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incisional hernia                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint dislocation                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tendon rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tibia fracture                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Toxicity to various agents                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper limb fracture                             |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaemia postoperative                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial bypass thrombosis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous graft site haemorrhage            |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Forearm fracture                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ulna fracture                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft complication                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular pseudoaneurysm                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervical vertebral fracture                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Concussion                                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Facial bones fracture                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritoneal dialysis complication                |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thoracic vertebral fracture                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acetabulum fracture                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Craniocerebral injury                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Fibula fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Foot fracture                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal stoma complication             |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Laceration                                      |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perirenal haematoma                             |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post-traumatic pain                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subdural haemorrhage                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Thermal burn                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound dehiscence                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound necrosis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wrist fracture                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous graft aneurysm                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous graft site haematoma              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Burns second degree                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clavicle fracture                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery restenosis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Extradural haematoma                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Face injury                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Graft haemorrhage                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ligament rupture                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Patella fracture                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative hernia                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural complication                         |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural intestinal perforation               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shunt aneurysm                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Shunt stenosis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin wound                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal fracture                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic haematoma                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular graft thrombosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal injury                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal wound dehiscence                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial bypass occlusion                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arterial injury                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arteriovenous fistula occlusion                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Avulsion fracture                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone contusion                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone fissure                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain contusion                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac valve replacement complication          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Complications of transplant surgery             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Complications of transplanted kidney            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Device deployment issue                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dislocation of vertebra                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eschar  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Extensive interdialytic weight gain             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fracture  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal anastomotic leak               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemodialysis complication                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyphaema  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incarcerated incisional hernia                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intentional overdose                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal anastomosis complication             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ligament sprain                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Kidney rupture                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lip injury                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Multiple injuries                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Muscle strain                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral artery restenosis                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural complication                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural haematuria                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative delirium                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative ileus                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postpericardiotomy syndrome                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural dizziness                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural hypertension                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural pain                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Procedural pneumothorax                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Radiation proctitis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Seroma  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skull fractured base                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenic injury                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenic rupture                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stoma site haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Stomal hernia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subcutaneous haematoma                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tendon injury                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic coma                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Traumatic haemorrhage                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Traumatic haemothorax                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Vascular access complication                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular bypass dysfunction                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vasoplegia syndrome                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound complication                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congenital, familial and genetic disorders      |                  |                  |  |
| Congenital cystic kidney disease                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydrocele                                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congenital bladder anomaly                      |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Nonketotic hyperglycinaemia                     |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Phimosi   |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cardiac disorders                               |                   |                   |  |
| Acute myocardial infarction                     |                   |                   |  |
| subjects affected / exposed                     | 63 / 1409 (4.47%) | 74 / 1409 (5.25%) |  |
| occurrences causally related to treatment / all | 3 / 82            | 3 / 94            |  |
| deaths causally related to treatment / all      | 0 / 10            | 0 / 17            |  |
| Atrial fibrillation                             |                   |                   |  |
| subjects affected / exposed                     | 49 / 1409 (3.48%) | 57 / 1409 (4.05%) |  |
| occurrences causally related to treatment / all | 0 / 58            | 0 / 66            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 3             |  |
| Myocardial infarction                           |                   |                   |  |
| subjects affected / exposed                     | 54 / 1409 (3.83%) | 50 / 1409 (3.55%) |  |
| occurrences causally related to treatment / all | 4 / 62            | 1 / 54            |  |
| deaths causally related to treatment / all      | 1 / 25            | 0 / 16            |  |
| Cardiac arrest                                  |                   |                   |  |
| subjects affected / exposed                     | 55 / 1409 (3.90%) | 44 / 1409 (3.12%) |  |
| occurrences causally related to treatment / all | 1 / 55            | 0 / 45            |  |
| deaths causally related to treatment / all      | 1 / 52            | 0 / 37            |  |
| Angina pectoris                                 |                   |                   |  |
| subjects affected / exposed                     | 35 / 1409 (2.48%) | 37 / 1409 (2.63%) |  |
| occurrences causally related to treatment / all | 0 / 37            | 1 / 46            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Cardiac failure                                 |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 25 / 1409 (1.77%) | 34 / 1409 (2.41%) |  |
| occurrences causally related to treatment / all | 0 / 31            | 0 / 37            |  |
| deaths causally related to treatment / all      | 0 / 12            | 0 / 13            |  |
| Acute coronary syndrome                         |                   |                   |  |
| subjects affected / exposed                     | 29 / 1409 (2.06%) | 25 / 1409 (1.77%) |  |
| occurrences causally related to treatment / all | 0 / 32            | 0 / 30            |  |
| deaths causally related to treatment / all      | 0 / 7             | 0 / 2             |  |
| Cardiac failure congestive                      |                   |                   |  |
| subjects affected / exposed                     | 20 / 1409 (1.42%) | 24 / 1409 (1.70%) |  |
| occurrences causally related to treatment / all | 0 / 24            | 0 / 26            |  |
| deaths causally related to treatment / all      | 0 / 4             | 0 / 4             |  |
| Coronary artery disease                         |                   |                   |  |
| subjects affected / exposed                     | 20 / 1409 (1.42%) | 24 / 1409 (1.70%) |  |
| occurrences causally related to treatment / all | 1 / 22            | 0 / 27            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Angina unstable                                 |                   |                   |  |
| subjects affected / exposed                     | 24 / 1409 (1.70%) | 16 / 1409 (1.14%) |  |
| occurrences causally related to treatment / all | 1 / 26            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Myocardial ischaemia                            |                   |                   |  |
| subjects affected / exposed                     | 17 / 1409 (1.21%) | 21 / 1409 (1.49%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 21            |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 6             |  |
| Bradycardia                                     |                   |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%)  | 20 / 1409 (1.42%) |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 21            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 3             |  |
| Cardio-respiratory arrest                       |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 12 / 1409 (0.85%) |  |
| occurrences causally related to treatment / all | 1 / 12            | 0 / 12            |  |
| deaths causally related to treatment / all      | 1 / 8             | 0 / 9             |  |
| Aortic valve stenosis                           |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 8 / 1409 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Atrioventricular block complete                 |                  |                  |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%) | 7 / 1409 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Coronary artery stenosis                        |                  |                  |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%) | 7 / 1409 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiogenic shock                               |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 9 / 1409 (0.64%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 5            | 0 / 7            |  |
| Atrial flutter                                  |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 9 / 1409 (0.64%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac failure acute                           |                  |                  |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |
| Cardiopulmonary failure                         |                  |                  |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 6            | 0 / 3            |  |
| Ventricular fibrillation                        |                  |                  |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 5            | 0 / 2            |  |
| Arrhythmia                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 7 / 1409 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |
| Left ventricular failure                        |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cardiac failure chronic                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atrioventricular block                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiomyopathy                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Sinus node dysfunction                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ventricular tachycardia                         |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic valve disease                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atrial tachycardia                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atrioventricular block second degree            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pericardial effusion                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pericarditis                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sinus bradycardia                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Acute left ventricular failure                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Arteriosclerosis coronary artery                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Atrial thrombosis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bradyarrhythmia                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery thrombosis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Ischaemic cardiomyopathy                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Right ventricular failure                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Tachyarrhythmia                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic valve disease mixed                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atrioventricular block first degree             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac disorder                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congestive cardiomyopathy                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery insufficiency                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mitral valve incompetence                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pericarditis uraemic                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulseless electrical activity                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Sinus tachycardia                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Supraventricular tachycardia                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ventricular extrasystoles                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Adams-Stokes syndrome                           |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aortic valve incompetence                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac dysfunction                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiac tamponade                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cardiovascular insufficiency                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Chordae tendinae rupture                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Conduction disorder                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Coronary artery dissection                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic cardiomyopathy                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Dressler's syndrome                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Extrasystoles                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Heart valve stenosis                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypertensive heart disease                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Mitral valve stenosis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myocarditis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Palpitations                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paroxysmal atrioventricular block               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pericardial haemorrhage                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Sinoatrial block                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Stress cardiomyopathy                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Tachycardia                                     |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Torsade de pointes                              |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tricuspid valve incompetence                    |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ventricular dyssynchrony                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ventricular tachyarrhythmia                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Nervous system disorders                        |                   |                   |  |
| Ischaemic stroke                                |                   |                   |  |
| subjects affected / exposed                     | 21 / 1409 (1.49%) | 28 / 1409 (1.99%) |  |
| occurrences causally related to treatment / all | 1 / 23            | 1 / 29            |  |
| deaths causally related to treatment / all      | 1 / 5             | 0 / 3             |  |
| Transient ischaemic attack                      |                   |                   |  |
| subjects affected / exposed                     | 30 / 1409 (2.13%) | 17 / 1409 (1.21%) |  |
| occurrences causally related to treatment / all | 2 / 31            | 0 / 21            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebrovascular accident                        |                   |                   |  |
| subjects affected / exposed                     | 24 / 1409 (1.70%) | 23 / 1409 (1.63%) |  |
| occurrences causally related to treatment / all | 0 / 27            | 4 / 26            |  |
| deaths causally related to treatment / all      | 0 / 10            | 0 / 4             |  |
| Syncope   |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 15 / 1409 (1.06%) | 22 / 1409 (1.56%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 27            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral haemorrhage                            |                   |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 5             | 0 / 5             |  |
| Seizure   |                   |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 10 / 1409 (0.71%) |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral infarction                             |                   |                   |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Dizziness                                       |                   |                   |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Carpal tunnel syndrome                          |                   |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Cerebral ischaemia                              |                   |                   |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 0             |  |
| Haemorrhagic stroke                             |                   |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 3             |  |
| Haemorrhage intracranial                        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 1 / 5            |  |
| deaths causally related to treatment / all      | 0 / 4            | 0 / 2            |  |
| Dementia  |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sciatica  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epilepsy  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Headache  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic encephalopathy                          |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Carotid artery stenosis                         |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vascular dementia                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebrovascular disorder                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Presyncope                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombotic stroke                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Altered state of consciousness                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral haematoma                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dementia Alzheimer's type                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Facial paralysis                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Stupor  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Aphasia   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ataxia  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain stem infarction                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dyskinesia                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Embolic stroke                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encephalopathy                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Generalised tonic-clonic seizure                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemic coma                              |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoxic-ischaemic encephalopathy                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intracranial aneurysm                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intraventricular haemorrhage                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Lacunar infarction                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peripheral sensorimotor neuropathy              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polyneuropathy                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Posterior reversible encephalopathy syndrome    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Trigeminal neuralgia                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Balance disorder                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Brain hypoxia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Brain injury                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cauda equina syndrome                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebellar stroke                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral ataxia                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebral arteriosclerosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Cerebral small vessel ischaemic disease         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cerebrovascular insufficiency                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cervical radiculopathy                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cognitive disorder                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dementia with Lewy bodies                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Demyelination                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Depressed level of consciousness                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic hyperosmolar coma                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic mononeuropathy                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic neuropathy                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Essential tremor                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Facial paresis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Guillain-Barre syndrome                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hemianopia homonymous                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hemiparesis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypocalcaemic seizure                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemic seizure                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoglycaemic unconsciousness                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| IIIrd nerve paralysis                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic neuropathy                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| IVth nerve paresis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lacunar stroke                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lethargy  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Loss of consciousness                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Memory impairment                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolic encephalopathy                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Migraine  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Monoparesis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Movement disorder                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myoclonic epilepsy                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nervous system disorder                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Noninfective encephalitis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Paraparesis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retrograde amnesia                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Reversible ischaemic neurological deficit       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Somnolence                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal subarachnoid haemorrhage                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Status epilepticus                              |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tension headache                                |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (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 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Transient global amnesia                        |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Unresponsive to stimuli                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vlth nerve paralysis                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Wallerian degeneration                          |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood and lymphatic system disorders            |                   |                   |  |
| Anaemia   |                   |                   |  |
| subjects affected / exposed                     | 25 / 1409 (1.77%) | 22 / 1409 (1.56%) |  |
| occurrences causally related to treatment / all | 1 / 27            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Haemolysis                                      |                   |                   |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombocytopenia                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone marrow failure                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Anaemia of chronic disease                      |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anaemia of malignant disease                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Disseminated intravascular coagulation          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Lymphadenopathy                                 |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nephrogenic anaemia                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spontaneous haematoma                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Thrombotic thrombocytopenic purpura             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone marrow toxicity                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Febrile bone marrow aplasia                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemolytic anaemia                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic anaemia                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Histiocytosis haematophagic                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Immune thrombocytopenic purpura                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Leukopenia                                      |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neutropenia                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Normochromic anaemia                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancytopenia                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polycythaemia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Splenic infarction                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spontaneous haemorrhage                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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                     |                  |                  |  |
| Vertigo   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sudden hearing loss                             |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Acute vestibular syndrome                       |                   |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Deafness unilateral                             |                   |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vertigo labyrinthine                            |                   |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Eye disorders                                   |                   |                  |  |
| Cataract  |                   |                  |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 9 / 1409 (0.64%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Vitreous haemorrhage                            |                   |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Glaucoma  |                   |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Diabetic retinopathy                            |                   |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| Retinal artery occlusion                        |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocrine ophthalmopathy                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ocular vasculitis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Optic ischaemic neuropathy                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Papilloedema                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retinal neovascularisation                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retinal vein thrombosis                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Vision blurred                                  |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Visual impairment                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vitreous haematoma                              |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastrointestinal disorders                      |                   |                   |  |
| Gastrointestinal haemorrhage                    |                   |                   |  |
| subjects affected / exposed                     | 24 / 1409 (1.70%) | 23 / 1409 (1.63%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 1 / 27            |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 3             |  |
| Abdominal pain                                  |                   |                   |  |
| subjects affected / exposed                     | 13 / 1409 (0.92%) | 16 / 1409 (1.14%) |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Diarrhoea                                       |                   |                   |  |
| subjects affected / exposed                     | 18 / 1409 (1.28%) | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 0 / 19            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Large intestine polyp                           |                   |                   |  |
| subjects affected / exposed                     | 9 / 1409 (0.64%)  | 10 / 1409 (0.71%) |  |
| occurrences causally related to treatment / all | 0 / 9             | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Rectal haemorrhage                              |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gastritis                                       |                   |                   |  |

|   |                   |                   |
|---|-------------------|-------------------|
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 11 / 1409 (0.78%) |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 11            |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |
| Constipation                                    |                   |                   |
| subjects affected / exposed                     | 7 / 1409 (0.50%)  | 8 / 1409 (0.57%)  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 8             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |
| Gastric ulcer                                   |                   |                   |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 5 / 1409 (0.35%)  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 5             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |
| Inguinal hernia                                 |                   |                   |
| subjects affected / exposed                     | 8 / 1409 (0.57%)  | 7 / 1409 (0.50%)  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 7             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |
| Colitis ischaemic                               |                   |                   |
| subjects affected / exposed                     | 7 / 1409 (0.50%)  | 7 / 1409 (0.50%)  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 7             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 3             |
| Gastric ulcer haemorrhage                       |                   |                   |
| subjects affected / exposed                     | 6 / 1409 (0.43%)  | 8 / 1409 (0.57%)  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 9             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 2             |
| Intestinal ischaemia                            |                   |                   |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 9 / 1409 (0.64%)  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 9             |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 5             |
| Intestinal obstruction                          |                   |                   |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 9 / 1409 (0.64%)  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 9             |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |
| Melaena   |                   |                   |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 1409 (0.50%) | 7 / 1409 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Colitis   |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 8 / 1409 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pancreatitis acute                              |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 9 / 1409 (0.64%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatitis                                    |                  |                  |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Duodenal ulcer haemorrhage                      |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Abdominal pain upper                            |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis erosive                               |                  |                  |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis haemorrhagic                          |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhoidal haemorrhage                       |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 1409 (0.50%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Umbilical hernia                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 7 / 1409 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Upper gastrointestinal haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Diverticulum                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum intestinal haemorrhagic            |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Enteritis                                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestinal obstruction                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Vomiting  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal angiodysplasia                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal angiodysplasia haemorrhagic    |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematemesis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Haemorrhoids                                    |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal infarction                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 4            |  |
| Gastrointestinal disorder                       |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematochezia                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mallory-Weiss syndrome                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic gastritis                               |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal ulcer                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dyspepsia                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric haemorrhage                             |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrooesophageal reflux disease                |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Incarcerated inguinal hernia                    |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large intestine perforation                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Abdominal discomfort                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subileus  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal wall haematoma                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute abdomen                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Anal fistula                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic gastroparesis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Encapsulating peritoneal sclerosis              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastric antral vascular ectasia                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroduodenitis                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal angiectasia                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal polyp haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhagic erosive gastritis                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileus   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Large intestinal ulcer haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Necrotising colitis                             |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophagitis                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatitis necrotising                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Peptic ulcer haemorrhage                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal prolapse                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal hernia                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ascites   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis erosive                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dental caries                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum intestinal                         |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocutaneous fistula                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erosive duodenitis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Erosive oesophagitis                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Food poisoning                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal necrosis                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal ulcer haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileus paralytic                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Incarcerated umbilical hernia                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal perforation                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal polyp                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large intestinal haemorrhage                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Large intestinal ulcer                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lower gastrointestinal haemorrhage              |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pancreatitis chronic                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritoneal perforation                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rectal polyp                                    |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal wall haemorrhage                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal stenosis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anal ulcer                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Anorectal varices                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendiceal mucocoele                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis ulcerative                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Defaecation urgency                             |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic gastropathy                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticular perforation                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diverticulum oesophageal                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenitis                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterocolitis haemorrhagic                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Faecaloma                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Flatulence                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gallstone ileus                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroduodenal ulcer                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal hypomotility                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ileal perforation                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Inguinal hernia strangulated                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal angina                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal mass                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal pseudo-obstruction                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal varices                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intra-abdominal fluid collection                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Irritable bowel syndrome                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ischaemic enteritis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Large intestinal stenosis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar hernia                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mesenteric arterial occlusion                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Nausea  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal spasm                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophageal ulcer                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oesophagitis haemorrhagic                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oral disorder                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peptic ulcer perforation                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Reflux gastritis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal haematoma                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal haemorrhage                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salivary gland enlargement                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Small intestinal haemorrhage                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tongue oedema                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Umbilical hernia, obstructive                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Varices oesophageal                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Volvulus  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Strangulated umbilical hernia                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin and subcutaneous tissue disorders          |                  |                  |  |
| Skin ulcer                                      |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 17 / 1409 (1.21%) | 17 / 1409 (1.21%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Diabetic foot                                   |                   |                   |  |
| subjects affected / exposed                     | 11 / 1409 (0.78%) | 13 / 1409 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 13            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Skin necrosis                                   |                   |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Ischaemic skin ulcer                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Drug eruption                                   |                   |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Decubitus ulcer                                 |                   |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 0 / 1409 (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 / 1409 (0.07%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Erythema  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Panniculitis                                    |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                           | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Pyoderma gangrenosum                                  |                  |                  |  |
| subjects affected / exposed                           | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Stasis dermatitis                                     |                  |                  |  |
| subjects affected / exposed                           | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Acute generalised exanthematous pustulosis            |                  |                  |  |
| subjects affected / exposed                           | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Cholestatic pruritus                                  |                  |                  |  |
| subjects affected / exposed                           | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Dermal cyst   |                  |                  |  |
| subjects affected / exposed                           | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Dermatitis exfoliative                                |                  |                  |  |
| subjects affected / exposed                           | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Diabetic ulcer  |                  |                  |  |
| subjects affected / exposed                           | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all            | 0 / 0            | 0 / 0            |  |
| Drug reaction with eosinophilia and systemic symptoms |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Erythema multiforme                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Henoch-Schonlein purpura                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hidradenitis                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperkeratosis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuropathic ulcer                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Psoriasis                                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin erosion                                    |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin lesion                                     |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urticaria                                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vasculitic rash                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal and urinary disorders                     |                   |                   |  |
| End stage renal disease                         |                   |                   |  |
| subjects affected / exposed                     | 26 / 1409 (1.85%) | 31 / 1409 (2.20%) |  |
| occurrences causally related to treatment / all | 0 / 26            | 0 / 31            |  |
| deaths causally related to treatment / all      | 0 / 26            | 0 / 29            |  |
| Renal impairment                                |                   |                   |  |
| subjects affected / exposed                     | 18 / 1409 (1.28%) | 20 / 1409 (1.42%) |  |
| occurrences causally related to treatment / all | 2 / 18            | 0 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Haematuria                                      |                   |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Chronic kidney disease                          |                   |                   |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%)  | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 1             |  |
| Azotaemia                                       |                   |                   |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Acute kidney injury                             |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Nephrolithiasis                                 |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal cyst haemorrhage                          |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hydronephrosis                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal failure                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Renal colic                                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary retention                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureteric stenosis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ureterolithiasis                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| 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                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bladder tamponade                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Calculus urethral                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystitis haemorrhagic                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystitis interstitial                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Glomerulonephritis                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemorrhage urinary tract                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Kidney enlargement                              |                  |                  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                        | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all         | 0 / 0            | 0 / 0            |  |
| Lupus nephritis                                    |                  |                  |  |
| subjects affected / exposed                        | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all    | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all         | 0 / 0            | 0 / 0            |  |
| Malnutrition-inflammation-atherosclerosis syndrome |                  |                  |  |
| subjects affected / exposed                        | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all         | 0 / 1            | 0 / 0            |  |
| Nephritis  |                  |                  |  |
| subjects affected / exposed                        | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all         | 0 / 0            | 0 / 0            |  |
| Nephropathy toxic                                  |                  |                  |  |
| subjects affected / exposed                        | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all         | 0 / 0            | 0 / 0            |  |
| Proteinuria  |                  |                  |  |
| subjects affected / exposed                        | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all         | 0 / 0            | 0 / 0            |  |
| Renal artery stenosis                              |                  |                  |  |
| subjects affected / exposed                        | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all         | 0 / 0            | 0 / 0            |  |
| Renal cyst ruptured                                |                  |                  |  |
| subjects affected / exposed                        | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all         | 0 / 0            | 0 / 0            |  |
| Renal haematoma                                    |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal ischaemia                                 |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Urethral stenosis                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary bladder haemorrhage                     |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract obstruction                       |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Endocrine disorders                             |                   |                   |  |
| Hyperparathyroidism secondary                   |                   |                   |  |
| subjects affected / exposed                     | 23 / 1409 (1.63%) | 19 / 1409 (1.35%) |  |
| occurrences causally related to treatment / all | 0 / 24            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyperparathyroidism tertiary                    |                   |                   |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hyperparathyroidism                             |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Adrenal insufficiency                           |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Goitre  |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 2 / 1409 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypothyroidism                                  |                   |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Basedow's disease                               |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Parathyroid hyperplasia                         |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 2 / 1409 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Musculoskeletal and connective tissue disorders |                   |                   |  |
| Osteoarthritis                                  |                   |                   |  |
| subjects affected / exposed                     | 16 / 1409 (1.14%) | 19 / 1409 (1.35%) |  |
| occurrences causally related to treatment / all | 0 / 17            | 0 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Musculoskeletal chest pain                      |                   |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Back pain                                       |                   |                   |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%)  | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Arthralgia                                      |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 6 / 1409 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral disc protrusion                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bursitis  |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteitis  |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal osteoarthritis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthritis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscular weakness                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Systemic lupus erythematosus                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gouty arthritis                                 |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemarthrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lumbar spinal stenosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pathological fracture                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polymyalgia rheumatica                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rhabdomyolysis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spinal column stenosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Synovitis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Joint effusion                                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Neuropathic arthropathy                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteolysis                                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteonecrosis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteoporotic fracture                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rotator cuff syndrome                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthrofibrosis                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Arthropathy                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all  | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Chronic kidney disease-mineral and bone disorder |                  |                  |  |
| subjects affected / exposed                      | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all  | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Collagen disorder                                |                  |                  |  |
| subjects affected / exposed                      | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Compartment syndrome                             |                  |                  |  |
| subjects affected / exposed                      | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Dupuytren's contracture                          |                  |                  |  |
| subjects affected / exposed                      | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Fibromyalgia                                     |                  |                  |  |
| subjects affected / exposed                      | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Flank pain                                       |                  |                  |  |
| subjects affected / exposed                      | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| High turnover osteopathy                         |                  |                  |  |
| subjects affected / exposed                      | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all       | 0 / 0            | 0 / 0            |  |
| Muscle haemorrhage                               |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Muscle necrosis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal pain                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myalgia   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Myositis  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pain in extremity                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Plantar fasciitis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Polyarthrititis                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rheumatoid arthritis                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sarcopenia                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Soft tissue necrosis                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Spondylitis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Sympathetic posterior cervical syndrome         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Torticollis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| Pneumonia                                       |                  |                  |  |

|   |                        |                        |  |
|---|------------------------|------------------------|--|
| subjects affected / exposed                     | 180 / 1409<br>(12.78%) | 163 / 1409<br>(11.57%) |  |
| occurrences causally related to treatment / all | 1 / 228                | 0 / 205                |  |
| deaths causally related to treatment / all      | 0 / 27                 | 0 / 19                 |  |
| Sepsis  |                        |                        |  |
| subjects affected / exposed                     | 69 / 1409 (4.90%)      | 85 / 1409 (6.03%)      |  |
| occurrences causally related to treatment / all | 0 / 79                 | 1 / 96                 |  |
| deaths causally related to treatment / all      | 0 / 26                 | 1 / 39                 |  |
| Peritonitis                                     |                        |                        |  |
| subjects affected / exposed                     | 47 / 1409 (3.34%)      | 46 / 1409 (3.26%)      |  |
| occurrences causally related to treatment / all | 0 / 62                 | 0 / 70                 |  |
| deaths causally related to treatment / all      | 0 / 2                  | 0 / 2                  |  |
| Septic shock                                    |                        |                        |  |
| subjects affected / exposed                     | 36 / 1409 (2.56%)      | 49 / 1409 (3.48%)      |  |
| occurrences causally related to treatment / all | 0 / 36                 | 0 / 50                 |  |
| deaths causally related to treatment / all      | 0 / 27                 | 0 / 34                 |  |
| Gastroenteritis                                 |                        |                        |  |
| subjects affected / exposed                     | 39 / 1409 (2.77%)      | 27 / 1409 (1.92%)      |  |
| occurrences causally related to treatment / all | 0 / 49                 | 0 / 27                 |  |
| deaths causally related to treatment / all      | 0 / 0                  | 0 / 0                  |  |
| Urinary tract infection                         |                        |                        |  |
| subjects affected / exposed                     | 31 / 1409 (2.20%)      | 33 / 1409 (2.34%)      |  |
| occurrences causally related to treatment / all | 0 / 35                 | 0 / 37                 |  |
| deaths causally related to treatment / all      | 0 / 0                  | 0 / 0                  |  |
| Device related sepsis                           |                        |                        |  |
| subjects affected / exposed                     | 21 / 1409 (1.49%)      | 30 / 1409 (2.13%)      |  |
| occurrences causally related to treatment / all | 0 / 29                 | 0 / 36                 |  |
| deaths causally related to treatment / all      | 0 / 2                  | 0 / 3                  |  |
| Lower respiratory tract infection               |                        |                        |  |
| subjects affected / exposed                     | 21 / 1409 (1.49%)      | 28 / 1409 (1.99%)      |  |
| occurrences causally related to treatment / all | 0 / 26                 | 0 / 37                 |  |
| deaths causally related to treatment / all      | 0 / 0                  | 0 / 2                  |  |
| Cellulitis                                      |                        |                        |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 22 / 1409 (1.56%) | 25 / 1409 (1.77%) |  |
| occurrences causally related to treatment / all | 0 / 25            | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Device related infection                        |                   |                   |  |
| subjects affected / exposed                     | 19 / 1409 (1.35%) | 28 / 1409 (1.99%) |  |
| occurrences causally related to treatment / all | 0 / 22            | 0 / 38            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Bronchitis                                      |                   |                   |  |
| subjects affected / exposed                     | 20 / 1409 (1.42%) | 24 / 1409 (1.70%) |  |
| occurrences causally related to treatment / all | 0 / 22            | 0 / 25            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Gangrene  |                   |                   |  |
| subjects affected / exposed                     | 22 / 1409 (1.56%) | 20 / 1409 (1.42%) |  |
| occurrences causally related to treatment / all | 0 / 24            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Respiratory tract infection                     |                   |                   |  |
| subjects affected / exposed                     | 16 / 1409 (1.14%) | 23 / 1409 (1.63%) |  |
| occurrences causally related to treatment / all | 0 / 19            | 0 / 25            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Staphylococcal sepsis                           |                   |                   |  |
| subjects affected / exposed                     | 14 / 1409 (0.99%) | 18 / 1409 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 20            |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 1             |  |
| Urosepsis                                       |                   |                   |  |
| subjects affected / exposed                     | 19 / 1409 (1.35%) | 11 / 1409 (0.78%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 5             | 0 / 1             |  |
| Bacteraemia                                     |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 14 / 1409 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Arteriovenous fistula site infection            |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 9 / 1409 (0.64%)  | 14 / 1409 (0.99%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Infection                                       |                   |                   |  |
| subjects affected / exposed                     | 15 / 1409 (1.06%) | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Upper respiratory tract infection               |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 10 / 1409 (0.71%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetic foot infection                         |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 0 / 14            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diverticulitis                                  |                   |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 13 / 1409 (0.92%) |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Erysipelas                                      |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 1 / 12            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Endocarditis                                    |                   |                   |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%)  | 10 / 1409 (0.71%) |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 2             |  |
| Catheter site infection                         |                   |                   |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%)  | 10 / 1409 (0.71%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Postoperative wound infection                   |                   |                   |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 10 / 1409 (0.71%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pyelonephritis                                  |                  |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Staphylococcal bacteraemia                      |                  |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Arteriovenous graft site infection              |                  |                   |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 7 / 1409 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Arthritis bacterial                             |                  |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Infected skin ulcer                             |                  |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Lung infection                                  |                  |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 8 / 1409 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1             |  |
| Viral infection                                 |                  |                   |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 1 / 8            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Pyelonephritis acute                            |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound infection                                 |                  |                  |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia sepsis                              |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Localised infection                             |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pneumonia bacterial                             |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pulmonary sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 7 / 1409 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 4            |  |
| Staphylococcal infection                        |                  |                  |  |
| subjects affected / exposed                     | 8 / 1409 (0.57%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Influenza                                       |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteomyelitis                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritonitis bacterial                           |                  |                  |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridium difficile colitis                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes zoster                                   |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Necrotising fasciitis                           |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Renal cyst infection                            |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendicitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 5 / 1409 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Cystitis  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                                   | 2 / 1409 (0.14%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all               | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Diabetic gangrene   |                  |                  |  |
| subjects affected / exposed                                   | 5 / 1409 (0.35%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all               | 0 / 6            | 0 / 1            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Enterococcal sepsis   |                  |                  |  |
| subjects affected / exposed                                   | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all               | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all                    | 0 / 2            | 0 / 0            |  |
| Infective exacerbation of chronic obstructive airways disease |                  |                  |  |
| subjects affected / exposed                                   | 3 / 1409 (0.21%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all               | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 1            |  |
| Abdominal abscess   |                  |                  |  |
| subjects affected / exposed                                   | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 1            |  |
| Abscess limb  |                  |                  |  |
| subjects affected / exposed                                   | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all               | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Anal abscess  |                  |                  |  |
| subjects affected / exposed                                   | 1 / 1409 (0.07%) | 4 / 1409 (0.28%) |  |
| occurrences causally related to treatment / all               | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Diverticulitis intestinal haemorrhagic                        |                  |                  |  |
| subjects affected / exposed                                   | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all               | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all                    | 0 / 0            | 0 / 0            |  |
| Infectious colitis  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infectious pleural effusion                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pseudomonal sepsis                              |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Soft tissue infection                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Biliary sepsis                                  |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fungal peritonitis                              |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Gastroenteritis viral                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Graft infection                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| H1N1 influenza                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infective exacerbation of bronchiectasis        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ophthalmic herpes zoster                        |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pseudomembranous colitis                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pyelonephritis chronic                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute sinusitis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cellulitis gangrenous                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholangitis infective                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cholecystitis infective                         |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis clostridial                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intervertebral discitis                         |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia staphylococcal                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural infection                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 3 / 1409 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Post procedural sepsis                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Pyonephrosis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Septic necrosis                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 1            |  |
| Sialoadenitis                                   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Streptococcal sepsis                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subcutaneous abscess                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tonsillitis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Wound sepsis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Abdominal sepsis                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Appendicitis perforated                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Arteriosclerotic gangrene                       |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atypical pneumonia                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial infection                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Clostridium difficile infection                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diarrhoea infectious                            |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Empyema   |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 0            |  |
| Encephalitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocarditis bacterial                          |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocarditis staphylococcal                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enterobacter sepsis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epididymitis                                    |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Epiglottitis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Fungal oesophagitis                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis salmonella                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Groin abscess                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haematoma infection                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemophilus infection                           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Joint tuberculosis                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Klebsiella sepsis                               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Listeriosis                                     |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lymph node tuberculosis                         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteomyelitis chronic                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumococcal sepsis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Pneumonia klebsiella                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Proteus infection                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pulmonary tuberculosis                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Renal graft infection                           |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Retroperitoneal abscess                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Septic arthritis staphylococcal                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 2            |  |
| Sinusitis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Staphylococcal skin infection                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Skin bacterial infection                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Streptococcal bacteraemia                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Systemic candida                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tuberculosis                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Urinary tract infection enterococcal            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal wall abscess                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Viral upper respiratory tract infection         |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abdominal wall infection                        |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Abscess jaw                                     |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Appendiceal abscess                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Atypical mycobacterial infection                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial colitis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacterial diarrhoea                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone abscess                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bone tuberculosis                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchitis viral                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bronchopulmonary aspergillosis                  |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Campylobacter gastroenteritis                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cat scratch disease                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Catheter site abscess                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cellulitis staphylococcal                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Chronic tonsillitis                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Citrobacter sepsis                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colon gangrene                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colonic abscess                                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Corneal abscess                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Corynebacterium sepsis                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Cystitis bacterial                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dacryocystitis                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Disseminated tuberculosis                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Endophthalmitis                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Enteritis infectious                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia infection                           |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia pyelonephritis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Escherichia urinary tract infection             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Febrile infection                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis bacterial                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis norovirus                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal infection                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Genitourinary tract infection                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hepatic cyst infection                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Herpes sepsis                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Herpes zoster meningoencephalitis               |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Implant site infection                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infected bunion                                 |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infected fistula                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infective gastroduodenitis                      |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Injection site infection                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Intestinal fistula infection                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Klebsiella infection                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Listeria encephalitis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Lung abscess                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Mesenteric abscess                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Mycetoma mycotic                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nail infection                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nasopharyngitis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nosocomial infection                            |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Oropharyngeal candidiasis                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Osteomyelitis acute                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis externa                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Otitis media acute                              |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Parotitis                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pelvic inflammatory disease                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Perihepatic abscess                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periodontitis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Periodontal destruction                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Peritonsillar abscess                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia legionella                            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pharyngitis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia necrotising                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia pseudomonal                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia respiratory syncytial viral           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Postoperative abscess                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pyomyositis                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Renal abscess                                   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory syncytial virus infection           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Rotavirus infection                             |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salmonellosis                                   |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Salpingitis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Seminal vesicle abscess                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Skin infection                                  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Staphylococcal abscess                          |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Subacute endocarditis                           |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tooth abscess                                   |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Tubo-ovarian abscess                            |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urethral abscess                                |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Urinary tract infection staphylococcal          |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Vaginal infection                               |                   |                   |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%)  | 1 / 1409 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Varicella                                       |                   |                   |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%)  | 0 / 1409 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Metabolism and nutrition disorders              |                   |                   |  |
| Fluid overload                                  |                   |                   |  |
| subjects affected / exposed                     | 43 / 1409 (3.05%) | 44 / 1409 (3.12%) |  |
| occurrences causally related to treatment / all | 1 / 52            | 0 / 50            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| Hyperkalaemia                                   |                   |                   |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 32 / 1409 (2.27%) | 18 / 1409 (1.28%) |  |
| occurrences causally related to treatment / all | 0 / 42            | 0 / 25            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 1             |  |
| Hypoglycaemia                                   |                   |                   |  |
| subjects affected / exposed                     | 17 / 1409 (1.21%) | 12 / 1409 (0.85%) |  |
| occurrences causally related to treatment / all | 0 / 19            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 1             |  |
| Cachexia  |                   |                   |  |
| subjects affected / exposed                     | 10 / 1409 (0.71%) | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 10            | 0 / 7             |  |
| Hyperglycaemia                                  |                   |                   |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%)  | 9 / 1409 (0.64%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| Dehydration                                     |                   |                   |  |
| subjects affected / exposed                     | 7 / 1409 (0.50%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Diabetes mellitus inadequate control            |                   |                   |  |
| subjects affected / exposed                     | 5 / 1409 (0.35%)  | 3 / 1409 (0.21%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Hypocalcaemia                                   |                   |                   |  |
| subjects affected / exposed                     | 6 / 1409 (0.43%)  | 2 / 1409 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Malnutrition                                    |                   |                   |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%)  | 4 / 1409 (0.28%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 0             |  |
| Hypervolaemia                                   |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Calciophylaxis                                  |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic complication                           |                  |                  |  |
| subjects affected / exposed                     | 4 / 1409 (0.28%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypercalcaemia                                  |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetes mellitus                               |                  |                  |  |
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyponatraemia                                   |                  |                  |  |
| subjects affected / exposed                     | 3 / 1409 (0.21%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gout  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Electrolyte imbalance                           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypokalaemia                                    |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 1409 (0.14%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hyperinsulinaemic hypoglycaemia                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 2 / 1409 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypovolaemia                                    |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Type 2 diabetes mellitus                        |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Decreased appetite                              |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic ketoacidosis                           |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Diabetic metabolic decompensation               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Fluid retention                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Haemochromatosis                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypoalbuminaemia                                |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Hypophosphataemia                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Lactic acidosis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| 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 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Metabolic disorder                              |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Mitochondrial cytopathy                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1409 (0.00%) | 1 / 1409 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Obesity   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Type 1 diabetes mellitus                        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1409 (0.07%) | 0 / 1409 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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

| <b>Non-serious adverse events</b>                     | Methoxy Polyethylene Glycol-Epoetin Beta | Erythropoiesis Stimulating Agents |  |
|---|--|-----------------------------------|--|
| Total subjects affected by non-serious adverse events |  |                                   |  |
| subjects affected / exposed                           | 1177 / 1409 (83.53%)                     | 1171 / 1409 (83.11%)              |  |
| Vascular disorders                                    |  |                                   |  |
| Hypertension  |  |                                   |  |
| subjects affected / exposed                           | 455 / 1409 (32.29%)                      | 432 / 1409 (30.66%)               |  |
| occurrences (all)                                     | 663                                      | 584                               |  |
| Hypotension   |  |                                   |  |
| subjects affected / exposed                           | 124 / 1409 (8.80%)                       | 143 / 1409 (10.15%)               |  |
| occurrences (all)                                     | 158                                      | 175                               |  |
| General disorders and administration site conditions  |  |                                   |  |
| Pyrexia   |  |                                   |  |
| subjects affected / exposed                           | 92 / 1409 (6.53%)                        | 96 / 1409 (6.81%)                 |  |
| occurrences (all)                                     | 107                                      | 115                               |  |
| Oedema due to renal disease                           |  |                                   |  |
| subjects affected / exposed                           | 78 / 1409 (5.54%)                        | 79 / 1409 (5.61%)                 |  |
| occurrences (all)                                     | 113                                      | 97                                |  |
| Asthenia  |  |                                   |  |
| subjects affected / exposed                           | 85 / 1409 (6.03%)                        | 59 / 1409 (4.19%)                 |  |
| occurrences (all)                                     | 100                                      | 67                                |  |
| Oedema peripheral                                     |  |                                   |  |
| subjects affected / exposed                           | 61 / 1409 (4.33%)                        | 73 / 1409 (5.18%)                 |  |
| occurrences (all)                                     | 67                                       | 79                                |  |
| Respiratory, thoracic and mediastinal disorders       |  |                                   |  |
| Cough   |  |                                   |  |
| subjects affected / exposed                           | 162 / 1409 (11.50%)                      | 194 / 1409 (13.77%)               |  |
| occurrences (all)                                     | 242                                      | 274                               |  |

|  |                            |                            |  |
|--|----------------------------|----------------------------|--|
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 109 / 1409 (7.74%)<br>129  | 109 / 1409 (7.74%)<br>132  |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 50 / 1409 (3.55%)<br>62    | 72 / 1409 (5.11%)<br>99    |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)  | 104 / 1409 (7.38%)<br>109  | 116 / 1409 (8.23%)<br>124  |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)   | 75 / 1409 (5.32%)<br>78    | 65 / 1409 (4.61%)<br>70    |  |
| Injury, poisoning and procedural complications<br>Procedural hypotension<br>subjects affected / exposed<br>occurrences (all) | 223 / 1409 (15.83%)<br>366 | 225 / 1409 (15.97%)<br>368 |  |
| Arteriovenous fistula site complication<br>subjects affected / exposed<br>occurrences (all)                                  | 158 / 1409 (11.21%)<br>231 | 171 / 1409 (12.14%)<br>262 |  |
| Arteriovenous fistula thrombosis<br>subjects affected / exposed<br>occurrences (all)   | 86 / 1409 (6.10%)<br>109   | 87 / 1409 (6.17%)<br>110   |  |
| Cardiac disorders<br>Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                                 | 111 / 1409 (7.88%)<br>125  | 123 / 1409 (8.73%)<br>154  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                                     | 141 / 1409 (10.01%)<br>199 | 127 / 1409 (9.01%)<br>187  |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)  | 81 / 1409 (5.75%)<br>100   | 78 / 1409 (5.54%)<br>86    |  |
| Blood and lymphatic system disorders   |                            |                            |  |

|  |                               |                               |  |
|--|-------------------------------|-------------------------------|--|
| Anaemia<br>subjects affected / exposed<br>occurrences (all)  | 174 / 1409<br>(12.35%)<br>205 | 143 / 1409<br>(10.15%)<br>176 |  |
| Eye disorders<br>Cataract<br>subjects affected / exposed<br>occurrences (all)                          | 76 / 1409 (5.39%)<br>87       | 72 / 1409 (5.11%)<br>82       |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 273 / 1409<br>(19.38%)<br>434 | 269 / 1409<br>(19.09%)<br>387 |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                                       | 142 / 1409<br>(10.08%)<br>162 | 173 / 1409<br>(12.28%)<br>205 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 121 / 1409 (8.59%)<br>162     | 146 / 1409<br>(10.36%)<br>197 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 104 / 1409 (7.38%)<br>137     | 99 / 1409 (7.03%)<br>121      |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 102 / 1409 (7.24%)<br>134     | 88 / 1409 (6.25%)<br>99       |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                               | 82 / 1409 (5.82%)<br>93       | 70 / 1409 (4.97%)<br>87       |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)  | 59 / 1409 (4.19%)<br>71       | 78 / 1409 (5.54%)<br>88       |  |
| Skin and subcutaneous tissue disorders<br>Pruritus<br>subjects affected / exposed<br>occurrences (all) | 114 / 1409 (8.09%)<br>128     | 118 / 1409 (8.37%)<br>136     |  |
| Endocrine disorders<br>Hyperparathyroidism secondary   |                               |                               |  |

|   |                        |                        |  |
|---|------------------------|------------------------|--|
| subjects affected / exposed                     | 148 / 1409<br>(10.50%) | 149 / 1409<br>(10.57%) |  |
| occurrences (all)                               | 165                    | 157                    |  |
| Musculoskeletal and connective tissue disorders |                        |                        |  |
| Muscle spasms                                   |                        |                        |  |
| subjects affected / exposed                     | 199 / 1409<br>(14.12%) | 211 / 1409<br>(14.98%) |  |
| occurrences (all)                               | 298                    | 311                    |  |
| Back pain                                       |                        |                        |  |
| subjects affected / exposed                     | 119 / 1409 (8.45%)     | 158 / 1409<br>(11.21%) |  |
| occurrences (all)                               | 140                    | 186                    |  |
| Pain in extremity                               |                        |                        |  |
| subjects affected / exposed                     | 124 / 1409 (8.80%)     | 133 / 1409 (9.44%)     |  |
| occurrences (all)                               | 170                    | 162                    |  |
| Arthralgia                                      |                        |                        |  |
| subjects affected / exposed                     | 125 / 1409 (8.87%)     | 110 / 1409 (7.81%)     |  |
| occurrences (all)                               | 150                    | 126                    |  |
| Osteoarthritis                                  |                        |                        |  |
| subjects affected / exposed                     | 86 / 1409 (6.10%)      | 105 / 1409 (7.45%)     |  |
| occurrences (all)                               | 93                     | 115                    |  |
| Musculoskeletal pain                            |                        |                        |  |
| subjects affected / exposed                     | 72 / 1409 (5.11%)      | 79 / 1409 (5.61%)      |  |
| occurrences (all)                               | 83                     | 99                     |  |
| Infections and infestations                     |                        |                        |  |
| Nasopharyngitis                                 |                        |                        |  |
| subjects affected / exposed                     | 187 / 1409<br>(13.27%) | 171 / 1409<br>(12.14%) |  |
| occurrences (all)                               | 389                    | 315                    |  |
| Bronchitis                                      |                        |                        |  |
| subjects affected / exposed                     | 188 / 1409<br>(13.34%) | 195 / 1409<br>(13.84%) |  |
| occurrences (all)                               | 295                    | 360                    |  |
| Urinary tract infection                         |                        |                        |  |
| subjects affected / exposed                     | 200 / 1409<br>(14.19%) | 193 / 1409<br>(13.70%) |  |
| occurrences (all)                               | 305                    | 293                    |  |
| Upper respiratory tract infection               |                        |                        |  |
| subjects affected / exposed                     | 132 / 1409 (9.37%)     | 153 / 1409<br>(10.86%) |  |
| occurrences (all)                               | 209                    | 266                    |  |



|                                    |                    |                     |  |
|------------------------------------|--------------------|---------------------|--|
| Gastroenteritis                    |                    |                     |  |
| subjects affected / exposed        | 101 / 1409 (7.17%) | 93 / 1409 (6.60%)   |  |
| occurrences (all)                  | 115                | 116                 |  |
| Pneumonia                          |                    |                     |  |
| subjects affected / exposed        | 79 / 1409 (5.61%)  | 101 / 1409 (7.17%)  |  |
| occurrences (all)                  | 101                | 116                 |  |
| Respiratory tract infection        |                    |                     |  |
| subjects affected / exposed        | 70 / 1409 (4.97%)  | 76 / 1409 (5.39%)   |  |
| occurrences (all)                  | 112                | 123                 |  |
| Lower respiratory tract infection  |                    |                     |  |
| subjects affected / exposed        | 74 / 1409 (5.25%)  | 55 / 1409 (3.90%)   |  |
| occurrences (all)                  | 135                | 105                 |  |
| Influenza                          |                    |                     |  |
| subjects affected / exposed        | 72 / 1409 (5.11%)  | 83 / 1409 (5.89%)   |  |
| occurrences (all)                  | 97                 | 111                 |  |
| Metabolism and nutrition disorders |                    |                     |  |
| Hyperkalaemia                      |                    |                     |  |
| subjects affected / exposed        | 122 / 1409 (8.66%) | 140 / 1409 (9.94%)  |  |
| occurrences (all)                  | 149                | 207                 |  |
| Hyperphosphataemia                 |                    |                     |  |
| subjects affected / exposed        | 136 / 1409 (9.65%) | 142 / 1409 (10.08%) |  |
| occurrences (all)                  | 157                | 163                 |  |
| Fluid overload                     |                    |                     |  |
| subjects affected / exposed        | 115 / 1409 (8.16%) | 130 / 1409 (9.23%)  |  |
| occurrences (all)                  | 136                | 178                 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 26 November 2008 | As a precautionary measure and to ensure that MIRCERA would be supplied within specifications, the protocol was amended so that only pre-filled syringes with a shelf-life of at least 24 months were used, as vials have limited stability. Additional strengths of pre-filled syringes were added.  |
| 15 November 2011 | Determination of cardiac markers at the time of suspected myocardial infarction was considered more appropriate than at pre-defined time points. The protocol was therefore amended to allow clinically meaningful assessment of this sampling while reducing the number of blood samples collected. Determination of coagulation parameters in case of hemorrhagic events was considered more appropriate than at pre-defined time points. |
| 23 March 2015    | Amendment to prolong the study by approximately 6 years (from the initial estimated duration of 4 years) because of a lower than anticipated event rate.  |

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.

|   |
|---|
| The study was designed and powered to formally test only the primary composite endpoint only. |
|---|

Notes: