



## Clinical trial results:

### Assessment of Clinical Effects of Cholesteryl Ester Transfer Protein Inhibition With Evacetrapib in Patients at a High-Risk for Vascular Outcomes

#### Summary

|                          |   |
|--------------------------|---|
| EudraCT number           | 2012-000061-21                                  |
| Trial protocol           | GB SK EE DE BE SE HU AT ES LT DK IT CZ PL BG NL |
| Global end of trial date | 19 July 2016                                    |

#### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 30 June 2018  |
| First version publication date | 06 March 2018   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Changes needed based on ClinicalTrials.gov changes. |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | I1V-MC-EIAN |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |   |
|------------------------------------|---|
| ISRCTN number                      | -   |
| ClinicalTrials.gov id (NCT number) | NCT01687998                                   |
| WHO universal trial number (UTN)   | -   |
| Other trial identifiers            | Trial Number: 11949, Trial Alias: I1V-MC-EIAN |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Eli Lilly and Company   |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285              |
| Public contact               | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,  |
| Scientific contact           | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559, |

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                       | 19 July 2016 |
| Is this the analysis of the primary completion data? | No           |

|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 19 July 2016 |
| Was the trial ended prematurely? | Yes          |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study is to test the hypothesis that evacetrapib 130 mg daily, in comparison to placebo, reduces the incidence of the composite endpoint of cardiovascular (CV) death, myocardial infarction (MI), stroke, coronary revascularization, or hospitalization for unstable angina (UA) in high-risk vascular disease (HRVD) participants.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 10 September 2012 |
| Long term follow-up planned                               | Yes               |
| Long term follow-up rationale                             | Safety, Efficacy  |
| Long term follow-up duration                              | 3 Years           |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Netherlands: 340    |
| Country: Number of subjects enrolled | Poland: 483         |
| Country: Number of subjects enrolled | Slovakia: 233       |
| Country: Number of subjects enrolled | Spain: 131          |
| Country: Number of subjects enrolled | Sweden: 66          |
| Country: Number of subjects enrolled | United Kingdom: 116 |
| Country: Number of subjects enrolled | Austria: 68         |
| Country: Number of subjects enrolled | Belgium: 84         |
| Country: Number of subjects enrolled | Bulgaria: 231       |
| Country: Number of subjects enrolled | Czech Republic: 372 |
| Country: Number of subjects enrolled | Denmark: 195        |
| Country: Number of subjects enrolled | Estonia: 59         |
| Country: Number of subjects enrolled | France: 97          |
| Country: Number of subjects enrolled | Germany: 400        |
| Country: Number of subjects enrolled | Hungary: 233        |
| Country: Number of subjects enrolled | Italy: 83           |
| Country: Number of subjects enrolled | Lithuania: 28       |

|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Russian Federation: 167 |
| Country: Number of subjects enrolled | Hong Kong: 52           |
| Country: Number of subjects enrolled | United States: 4475     |
| Country: Number of subjects enrolled | China: 445              |
| Country: Number of subjects enrolled | Korea, Republic of: 181 |
| Country: Number of subjects enrolled | Brazil: 110             |
| Country: Number of subjects enrolled | Argentina: 180          |
| Country: Number of subjects enrolled | Romania: 130            |
| Country: Number of subjects enrolled | Japan: 407              |
| Country: Number of subjects enrolled | Ukraine: 133            |
| Country: Number of subjects enrolled | Switzerland: 29         |
| Country: Number of subjects enrolled | New Zealand: 127        |
| Country: Number of subjects enrolled | Canada: 1245            |
| Country: Number of subjects enrolled | Turkey: 3               |
| Country: Number of subjects enrolled | Taiwan: 105             |
| Country: Number of subjects enrolled | Mexico: 466             |
| Country: Number of subjects enrolled | South Africa: 153       |
| Country: Number of subjects enrolled | Israel: 146             |
| Country: Number of subjects enrolled | Australia: 319          |
| Worldwide total number of subjects   | 12092                   |
| EEA total number of subjects         | 3349                    |

Notes:

### Subjects enrolled per age group

|   |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 5713 |
| From 65 to 84 years                       | 6278 |
| 85 years and over                         | 101  |

## Subject disposition

### Recruitment

Recruitment details:

No Text Entered

### Pre-assignment

Screening details:

Non-Completers: Participants "Known to be Alive at Study End" is a subset of those who did not withdraw consent and later found to be alive from public sources. "Lost to follow-up" is a subset of those who did not withdraw consent for whom study end vital status could not be ascertained.

### Period 1

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

### Arms

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

Arm description:

Evacetrapib 130 milligram (mg) tablet, administered orally once daily for up to 4 years. Participants will also receive standard of care for high-risk vascular disease (HRVD).

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Evacetrapib  |
| Investigational medicinal product code |              |
| Other name                             | LY2484595    |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Evacetrapib 130 mg tablet, administered orally once daily for up to 4 years. Participants will also receive standard of care for high-risk vascular disease (HRVD).

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

Arm description:

Placebo, tablet administered orally once daily for up to 4 years. Participants will also receive standard of care for HRVD.

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

Dosage and administration details:

Placebo, tablet administered orally once daily for up to 4 years. Participants received standard of care for HRVD.

| <b>Number of subjects in period 1</b>    | Evacetrapib | Placebo |
|--|-------------|---------|
| Started                                  | 6038        | 6054    |
| Received at Least One Dose of Study Drug | 6036        | 6052    |
| Completed                                | 5926        | 5934    |
| Not completed                            | 112         | 120     |
| Consent withdrawn by subject             | 49          | 51      |
| Known to be Alive at Study End           | 54          | 62      |
| Lost to follow-up                        | 9           | 7       |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                             | Overall Study | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 12092         | 12092 |  |
| Age categorical                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| In utero   | 0             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                               | 0             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0             | 0     |  |
| Children (2-11 years)                              | 0             | 0     |  |
| Adolescents (12-17 years)                          | 0             | 0     |  |
| Adults (18-64 years)                               | 5713          | 5713  |  |
| From 65-84 years                                   | 6278          | 6278  |  |
| 85 years and over                                  | 101           | 101   |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 2784          | 2784  |  |
| Male   | 9308          | 9308  |  |
| Race   |               |       |  |
| Units: Subjects                                    |               |       |  |
| American Indian or Alaska Native                   | 469           | 469   |  |
| Asian  | 1290          | 1290  |  |
| Native Hawaiian or Other Pacific Islander          | 11            | 11    |  |
| Black or African American                          | 294           | 294   |  |
| White  | 9904          | 9904  |  |
| More than one race                                 | 61            | 61    |  |
| Unknown or Not Reported                            | 63            | 63    |  |
| Ethnicity  |               |       |  |
| Units: Subjects                                    |               |       |  |
| Hispanic or Latino                                 | 1022          | 1022  |  |
| Not Hispanic or Latino                             | 10780         | 10780 |  |
| Unknown or Not Reported                            | 290           | 290   |  |

## End points

### End points reporting groups

|   |             |
|---|-------------|
| Reporting group title   | Evacetrapib |
| Reporting group description:<br>Evacetrapib 130 milligram (mg) tablet, administered orally once daily for up to 4 years. Participants will also receive standard of care for high-risk vascular disease (HRVD). |             |
| Reporting group title   | Placebo     |
| Reporting group description:<br>Placebo, tablet administered orally once daily for up to 4 years. Participants will also receive standard of care for HRVD.   |             |

### Primary: Number of Participants With Composite Primary Endpoint of Cardiovascular (CV) Death, Myocardial Infarction (MI), Stroke, Coronary Revascularization, or Hospitalization for Unstable Angina (UA)

|  |  |
|--|--|
| End point title  | Number of Participants With Composite Primary Endpoint of Cardiovascular (CV) Death, Myocardial Infarction (MI), Stroke, Coronary Revascularization, or Hospitalization for Unstable Angina (UA) |
| End point description:<br>For component endpoints, the number of participants includes those experiencing fatal events and account for all occurrences regardless of whether or not another component event occurred previously. |  |
| End point type   | Primary  |
| End point timeframe:<br>Baseline to Study Completion (Up to 4 years)   |  |

| End point values            | Evacetrapib         | Placebo             |  |  |
|-----------------------------|---------------------|---------------------|--|--|
| Subject group type          | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed | 6038 <sup>[1]</sup> | 6054 <sup>[2]</sup> |  |  |
| Units: participants         | 779                 | 776                 |  |  |

Notes:

[1] - All randomized participants.

[2] - All randomized participants.

### Statistical analyses

|  |   |
|--|---|
| Statistical analysis title   | Statistical Analysis Composite Primary Endpoint |
| Statistical analysis description:<br>Primary Endpoint: Time to First Occurrence of the Composite Primary Endpoint of Cardiovascular (CV) Death, Myocardial Infarction (MI), Stroke, Coronary Revascularization, or Hospitalization for Unstable Angina (UA). |   |
| Comparison groups  | Evacetrapib v Placebo                           |

|   |                   |
|---|-------------------|
| Number of subjects included in analysis | 12092             |
| Analysis specification                  | Pre-specified     |
| Analysis type                           | superiority       |
| P-value                                 | = 0.9054          |
| Method                                  | Regression, Cox   |
| Parameter estimate                      | Hazard ratio (HR) |
| Point estimate                          | 1.006             |
| Confidence interval                     |                   |
| level                                   | 95 %              |
| sides                                   | 2-sided           |
| lower limit                             | 0.911             |
| upper limit                             | 1.111             |

### Secondary: Mean Percent Change From Baseline to 3 Months in Low-Density (LDL-C) and High-Density Lipoprotein Cholesterol (HDL-C) Levels

|                        |  |
|------------------------|--|
| End point title        | Mean Percent Change From Baseline to 3 Months in Low-Density (LDL-C) and High-Density Lipoprotein Cholesterol (HDL-C) Levels |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| Baseline, 3 Months     |  |

| End point values                     | Evacetrapib         | Placebo             |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type                   | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed          | 6038 <sup>[3]</sup> | 6054 <sup>[4]</sup> |  |  |
| Units: Percent                       |                     |                     |  |  |
| arithmetic mean (standard deviation) |                     |                     |  |  |
| LDL-C (n=5760, 5786)                 | -31.12 (± 27.583)   | -5.99 (± 29.007)    |  |  |
| HDL-C (n=5760, 5788)                 | 133.18 (± 57.204)   | 1.63 (± 17.455)     |  |  |

Notes:

[3] - All randomized participants with evaluable LDL-C levels.

[4] - All randomized participants with evaluable HDL-C levels.

### Statistical analyses

|   |                                       |
|---|---------------------------------------|
| Statistical analysis title              | Statistical Analysis for LDL-C Levels |
| Comparison groups                       | Placebo v Evacetrapib                 |
| Number of subjects included in analysis | 12092                                 |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | < 0.0001                              |
| Method                                  | ANOVA                                 |
| Parameter estimate                      | Mean difference (final values)        |
| Point estimate                          | -37.11                                |



|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | -38.15  |
| upper limit         | -36.08  |

|   |                                       |
|---|---------------------------------------|
| <b>Statistical analysis title</b>       | Statistical Analysis for HDL-C Levels |
| Comparison groups                       | Evacetrapib v Placebo                 |
| Number of subjects included in analysis | 12092                                 |
| Analysis specification                  | Pre-specified                         |
| Analysis type                           | superiority                           |
| P-value                                 | < 0.0001                              |
| Method                                  | ANOVA                                 |
| Parameter estimate                      | Mean difference (final values)        |
| Point estimate                          | 131.55                                |
| Confidence interval                     |                                       |
| level                                   | 95 %                                  |
| sides                                   | 2-sided                               |
| lower limit                             | 130.01                                |
| upper limit                             | 133.09                                |

**Secondary: Number of Participants With Composite Endpoint of All-Cause Mortality, MI, Stroke, Coronary Revascularization, or Hospitalization for UA**

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Composite Endpoint of All-Cause Mortality, MI, Stroke, Coronary Revascularization, or Hospitalization for UA |
|-----------------|--|

End point description:

For component endpoints, the number of participants includes those experiencing fatal events and account for all occurrences regardless of whether or not another component event occurred previously.

|   |           |
|---|-----------|
| End point type                                | Secondary |
| End point timeframe:                          |           |
| Baseline through End of Study (Up to 4 years) |           |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | Evacetrapib     | Placebo         |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 6038            | 6054            |  |  |
| Units: participants         | 857             | 867             |  |  |

## Statistical analyses

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis Composite Endpoint Mortality |
| Statistical analysis description:<br>Time to First Occurrence of the Composite Endpoint of All-Cause Mortality, MI, Stroke, Coronary Revascularization, or Hospitalization for UA. |   |
| Comparison groups  | Evacetrapib v Placebo                             |
| Number of subjects included in analysis  | 12092   |
| Analysis specification   | Pre-specified                                     |
| Analysis type  | superiority                                       |
| P-value  | = 0.8463  |
| Method   | Regression, Cox                                   |
| Parameter estimate   | Hazard ratio (HR)                                 |
| Point estimate   | 0.991   |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 0.901   |
| upper limit  | 1.089   |

## Secondary: Number of Participants With Composite Endpoint of CV Death, MI, or Coronary Revascularization

|  |   |
|--|---|
| End point title  | Number of Participants With Composite Endpoint of CV Death, MI, or Coronary Revascularization |
| End point description:<br>For component endpoints, the number of participants includes those experiencing fatal events and account for all occurrences regardless of whether or not another component event occurred previously. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline through End of Study (Up to 4 years)  |   |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | Evacetrapib     | Placebo         |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 6038            | 6054            |  |  |
| Units: participants         | 690             | 691             |  |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis for CV Death, MI, or Coronary |
| Statistical analysis description:<br>Time to First Occurrence of the Composite Endpoint of CV Death, MI, or Coronary Revascularization |  |
| Comparison groups  | Placebo v Evacetrapib                              |

|   |                   |
|---|-------------------|
| Number of subjects included in analysis | 12092             |
| Analysis specification                  | Pre-specified     |
| Analysis type                           | superiority       |
| P-value                                 | = 0.9874          |
| Method                                  | Regression, Cox   |
| Parameter estimate                      | Hazard ratio (HR) |
| Point estimate                          | 1.001             |
| Confidence interval                     |                   |
| level                                   | 95 %              |
| sides                                   | 2-sided           |
| lower limit                             | 0.901             |
| upper limit                             | 1.112             |

### Secondary: Number of Participants With Composite Endpoint of CV Death, MI, Stroke, or Hospitalization for UA

|  |   |
|--|---|
| End point title  | Number of Participants With Composite Endpoint of CV Death, MI, Stroke, or Hospitalization for UA |
| End point description:   |   |
| For component endpoints, the number of participants includes those experiencing fatal events and account for all occurrences regardless of whether or not another component event occurred previously. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline through End of Study (Up to 4 years)  |   |

| End point values            | Evacetrapib     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 6038            | 6054            |  |  |
| Units: participants         | 571             | 570             |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title  | Statistical Analysis for CV Death, MI, Stroke |
| Statistical analysis description:   |   |
| Time to First Occurrence of the Composite Endpoint of CV Death, MI, Stroke, or Hospitalization for UA |   |
| Comparison groups   | Evacetrapib v Placebo                         |
| Number of subjects included in analysis   | 12092   |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | superiority                                   |
| P-value   | = 0.9574                                      |
| Method  | Regression, Cox                               |
| Parameter estimate  | Hazard ratio (HR)                             |
| Point estimate  | 1.003   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.893   |
| upper limit         | 1.127   |

## Secondary: Number of Participants With Triple Composite Endpoint of CV Death, MI, or Stroke

|  |  |
|--|--|
| End point title  | Number of Participants With Triple Composite Endpoint of CV Death, MI, or Stroke |
| End point description:   |  |
| For component endpoints, the number of participants includes those experiencing fatal events and account for all occurrences regardless of whether or not another component event occurred previously. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline through End of Study (Up to 4 years)  |  |

| End point values            | Evacetrapib     | Placebo         |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 6038            | 6054            |  |  |
| Units: participants         | 437             | 453             |  |  |

## Statistical analyses

|   |   |
|---|---|
| Statistical analysis title  | Statistical Analysis for Triple Composite |
| Statistical analysis description:   |   |
| Time to First Occurrence of Triple Composite Endpoint of CV Death, MI, or Stroke. |   |
| Comparison groups   | Evacetrapib v Placebo                     |
| Number of subjects included in analysis   | 12092                                     |
| Analysis specification  | Pre-specified                             |
| Analysis type   | superiority                               |
| P-value   | = 0.5917                                  |
| Method  | Regression, Cox                           |
| Parameter estimate  | Hazard ratio (HR)                         |
| Point estimate  | 0.965                                     |
| Confidence interval   |   |
| level   | 95 %                                      |
| sides   | 2-sided                                   |
| lower limit   | 0.846                                     |
| upper limit   | 1.1                                       |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

I1V-MC-EIAN

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 15.1 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Evacetrapib |
|-----------------------|-------------|

Reporting group description:

Evacetrapib 130 milligram (mg) tablet, administered orally once daily for up to 4 years. Participants will also receive standard of care for high-risk vascular disease (HRVD).

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

Reporting group description:

Placebo tablet administered orally once daily for up to 4 years. Participants will also receive standard of care for HRVD.

| Serious adverse events  | Evacetrapib             | Placebo                 |  |
|---|-------------------------|-------------------------|--|
| Total subjects affected by serious adverse events                   |                         |                         |  |
| subjects affected / exposed   | 2306 / 6036<br>(38.20%) | 2341 / 6052<br>(38.68%) |  |
| number of deaths (all causes)                                       | 240                     | 287                     |  |
| number of deaths resulting from adverse events                      | 8                       | 5                       |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                         |                         |  |
| acute myeloid leukaemia   |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1                         |                         |                         |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)        | 1 / 6052 (0.02%)        |  |
| occurrences causally related to treatment / all                     | 0 / 1                   | 0 / 1                   |  |
| deaths causally related to treatment / all                          | 0 / 1                   | 0 / 1                   |  |
| adenocarcinoma  |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1                         |                         |                         |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)        | 0 / 6052 (0.00%)        |  |
| occurrences causally related to treatment / all                     | 0 / 2                   | 0 / 0                   |  |
| deaths causally related to treatment / all                          | 0 / 1                   | 0 / 0                   |  |
| adenocarcinoma gastric  |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1                         |                         |                         |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                               | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all                                    | 0 / 1            | 0 / 1            |  |
| adenocarcinoma of colon<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all                               | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| adenocarcinoma pancreas<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                               | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| adenosquamous cell lung cancer<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                    | 0 / 1            | 0 / 0            |  |
| anal squamous cell carcinoma<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                               | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| anaplastic astrocytoma<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                               | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| b-cell lymphoma<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                               | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |

|  |                   |                   |  |  |
|--|-------------------|-------------------|--|--|
| b-cell lymphoma stage iv<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed         | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1             | 0 / 0             |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |  |
| basal cell carcinoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed             | 17 / 6036 (0.28%) | 13 / 6052 (0.21%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 17            | 0 / 16            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |  |
| basosquamous carcinoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed           | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0             | 0 / 1             |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |  |
| benign gastric neoplasm<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed          | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1             | 0 / 0             |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |  |
| benign neoplasm of spinal cord<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1             | 0 / 0             |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |  |
| benign neoplasm of adrenal gland<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1             | 0 / 0             |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |  |
| benign neoplasm of thyroid gland<br>alternative dictionary used:<br>MedDRA 15.1                                |                   |                   |  |  |

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| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| benign renal neoplasm<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| bladder cancer<br>alternative dictionary used:<br>MedDRA 15.1                      |                  |                  |  |
| subjects affected / exposed  | 8 / 6036 (0.13%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                                    | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| bladder cancer recurrent<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| bladder neoplasm<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| bladder transitional cell carcinoma<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 4 / 6036 (0.07%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all                                    | 0 / 4            | 0 / 7            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| borderline mucinous tumour of ovary<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |



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| bowen's disease<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 3            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| breast cancer<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |  |
| subjects affected / exposed  | 6 / 6036 (0.10%) | 4 / 6052 (0.07%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 6            | 0 / 4            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| breast cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 0            | 1 / 1            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| bronchial carcinoma<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                         | 1 / 2            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all                              | 1 / 1            | 0 / 1            |  |  |
| bronchial neoplasm<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 0            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| burkitt's lymphoma<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 1            | 0 / 0            |  |  |
| buschke-lowenstein's tumour<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |

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|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| carcinoid tumour                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| carcinoid tumour of the gastrointestinal tract  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cervix carcinoma stage 0                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[1]</sup>      | 1 / 1388 (0.07%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cholangiocarcinoma                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0            |  |
| chronic lymphocytic leukaemia                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| chronic lymphocytic leukaemia stage 0           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

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|--|------------------|------------------|--|
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| chronic myeloid leukaemia<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| colon adenoma<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |
| subjects affected / exposed  | 5 / 6036 (0.08%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                          | 1 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| colon cancer<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |
| subjects affected / exposed  | 4 / 6036 (0.07%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all                          | 1 / 4            | 0 / 7            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| colon cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all                               | 0 / 1            | 0 / 1            |  |
| colon cancer stage 0<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| colon cancer stage iii<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |

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|---|------------------|------------------|--|--|
| colon cancer stage iv<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed         | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| colorectal cancer<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed             | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 3            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| colorectal cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| colorectal cancer stage iv<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed    | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| desmoplastic melanoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed         | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| diffuse large b-cell lymphoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| diffuse large b-cell lymphoma<br>recurrent<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |  |

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| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| diffuse large b-cell lymphoma stage ii          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| diffuse large b-cell lymphoma stage iii         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| endometrial adenocarcinoma                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ewing's sarcoma metastatic                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| fallopian tube cancer                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[2]</sup>      | 0 / 6036 (0.00%) | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| fibrous histiocytoma                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

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|---|------------------|------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| gallbladder adenocarcinoma<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| gastric adenoma<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                   | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| gastric cancer<br>alternative dictionary used:<br>MedDRA 15.1                     |                  |                  |  |
| subjects affected / exposed   | 4 / 6036 (0.07%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all                                   | 2 / 5            | 1 / 7            |  |
| deaths causally related to treatment / all  | 1 / 1            | 0 / 2            |  |
| gastrointestinal cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| gastrointestinal stromal tumour<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                   | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| gastrointestinal tract adenoma<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |

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| gastroesophageal cancer<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                       | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                            | 0 / 0            | 0 / 1            |  |
| gingival cancer<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                       | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                            | 0 / 0            | 0 / 0            |  |
| glioblastoma<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all                       | 0 / 3            | 0 / 4            |  |
| deaths causally related to<br>treatment / all                            | 0 / 1            | 0 / 0            |  |
| haemangioma of liver<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                       | 0 / 0            | 1 / 1            |  |
| deaths causally related to<br>treatment / all                            | 0 / 0            | 0 / 0            |  |
| hepatic cancer<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all                       | 0 / 0            | 0 / 3            |  |
| deaths causally related to<br>treatment / all                            | 0 / 0            | 0 / 1            |  |
| hepatic cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                       | 0 / 2            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                            | 0 / 0            | 0 / 1            |  |
| hepatocellular carcinoma<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |

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| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| hodgkin's disease                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hodgkin's disease stage iv                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| intestinal adenocarcinoma                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| invasive breast carcinoma                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| invasive lobular breast carcinoma               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| invasive ductal breast carcinoma                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |



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|--|---|---|--|--|
| <p>kaposi's sarcoma</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>  | <p>1 / 6036 (0.02%)</p> <p>0 / 1</p> <p>0 / 0</p> | <p>1 / 6052 (0.02%)</p> <p>0 / 1</p> <p>0 / 0</p> |  |  |
| <p>keratinising squamous cell carcinoma<br/>of nasopharynx</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p> | <p>1 / 6036 (0.02%)</p> <p>0 / 1</p> <p>0 / 1</p> | <p>0 / 6052 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |
| <p>keratoacanthoma</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>   | <p>1 / 6036 (0.02%)</p> <p>0 / 1</p> <p>0 / 0</p> | <p>0 / 6052 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |
| <p>large intestine benign neoplasm</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>                         | <p>1 / 6036 (0.02%)</p> <p>0 / 1</p> <p>0 / 0</p> | <p>0 / 6052 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |
| <p>laryngeal cancer</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>  | <p>1 / 6036 (0.02%)</p> <p>0 / 1</p> <p>0 / 0</p> | <p>0 / 6052 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |
| <p>laryngeal neoplasm</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>                                      | <p>1 / 6036 (0.02%)</p> <p>0 / 1</p> <p>0 / 0</p> | <p>0 / 6052 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |
| <p>laryngeal squamous cell carcinoma</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p>   |   |   |  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                              | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                   | 0 / 0            | 0 / 0            |  |
| lip squamous cell carcinoma<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                              | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                   | 0 / 0            | 0 / 0            |  |
| lipoma<br>alternative dictionary used:<br>MedDRA 15.1                        |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                              | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                   | 0 / 0            | 0 / 0            |  |
| lung adenocarcinoma<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed  | 7 / 6036 (0.12%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all                              | 0 / 7            | 0 / 8            |  |
| deaths causally related to treatment / all                                   | 0 / 2            | 0 / 5            |  |
| lung adenocarcinoma stage i<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                              | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                   | 0 / 0            | 0 / 0            |  |
| lung adenocarcinoma stage ii<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                              | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                   | 0 / 0            | 0 / 0            |  |
| lung adenocarcinoma stage iii<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                              | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                   | 0 / 0            | 0 / 0            |  |

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|---|------------------|------------------|--|
| lung cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all                    | 0 / 2            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                         | 0 / 2            | 0 / 1            |  |
| lung carcinoma cell type unspecified<br>recurrent                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1                           |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                    | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                         | 0 / 0            | 0 / 0            |  |
| lung carcinoma cell type unspecified<br>stage ii                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1                           |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                    | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                         | 0 / 0            | 0 / 0            |  |
| lung carcinoma cell type unspecified<br>stage iii                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1                           |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                    | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                         | 0 / 0            | 0 / 0            |  |
| lung carcinoma cell type unspecified<br>stage iv                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1                           |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all                    | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                         | 0 / 0            | 0 / 2            |  |
| lung neoplasm   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1                           |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                         | 0 / 0            | 0 / 0            |  |
| lung neoplasm malignant   |                  |                  |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 14 / 6036 (0.23%) | 13 / 6052 (0.21%) |  |
| occurrences causally related to<br>treatment / all | 0 / 15            | 1 / 13            |  |
| deaths causally related to<br>treatment / all      | 0 / 7             | 1 / 8             |  |
| lung squamous cell carcinoma<br>metastatic         |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| lung squamous cell carcinoma stage i               |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| lung squamous cell carcinoma stage<br>iii          |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| lymphocytic lymphoma                               |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| lymphoma   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to<br>treatment / all      | 0 / 1             | 0 / 2             |  |
| malignant fibrous histiocytoma                     |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| malignant melanoma                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| malignant melanoma in situ                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| malignant neoplasm of unknown primary site      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| malignant neoplasm progression                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| malignant pleural effusion                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| mediastinum neoplasm                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| meningioma                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| meningioma malignant                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| metastases to bone                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| metastases to central nervous system            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| metastases to liver                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| metastases to lymph nodes                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                   | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| metastases to lung<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                                   | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| metastases to salivary gland<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| metastatic malignant melanoma<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                   | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all  | 0 / 1            | 0 / 1            |  |
| metastatic squamous cell carcinoma<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| myelodysplastic syndrome<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                   | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 1            |  |
| myxofibrosarcoma<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |

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|--|------------------|------------------|--|--|
| nasal sinus cancer<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| nasopharyngeal cancer<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| neoplasm progression<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| neoplasm prostate<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[3]</sup>       | 0 / 6036 (0.00%) | 1 / 4658 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| neoplasm skin<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                          | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| neuroendocrine carcinoma<br>metastatic<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 2            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 2            | 0 / 0            |  |  |
| neuroendocrine tumour<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                      | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 1            | 0 / 0            |  |
| non-hodgkin's lymphoma<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| non-small cell lung cancer<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                      | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 2            | 0 / 0            |  |
| non-small cell lung cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                      | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| non-small cell lung cancer stage iii<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| non-small cell lung cancer stage iiia<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| non-small cell lung cancer stage iv<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                      | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 1            | 0 / 0            |  |

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|---|------------------|------------------|--|--|
| oesophageal adenocarcinoma<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                                      | 0 / 3            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| oesophageal adenocarcinoma<br>metastatic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                      | 2 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 1 / 1            | 0 / 1            |  |  |
| oesophageal adenocarcinoma stage<br>0<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                                      | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| oesophageal carcinoma<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                      | 0 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |  |
| oral cavity cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                      | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| oropharyngeal cancer<br>alternative dictionary used:<br>MedDRA 15.1                     |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                      | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| oropharyngeal squamous cell<br>carcinoma<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                       | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| pancreatic carcinoma<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all                                       | 0 / 3            | 1 / 8            |  |
| deaths causally related to treatment / all  | 0 / 2            | 0 / 3            |  |
| pancreatic carcinoma metastatic<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                       | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all  | 0 / 1            | 0 / 1            |  |
| pancreatic neoplasm<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                       | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| pancreatic neuroendocrine tumour<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| papillary cystadenoma<br>lymphomatosum<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                       | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all  | 0 / 0            | 0 / 0            |  |
| papillary thyroid cancer<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| subjects affected / exposed  | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                          | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| parathyroid tumour benign<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed  | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                          | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| phaeochromocytoma<br>alternative dictionary used:<br>MedDRA 15.1         |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                          | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| pituitary tumour<br>alternative dictionary used:<br>MedDRA 15.1          |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                          | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| plasma cell myeloma<br>alternative dictionary used:<br>MedDRA 15.1       |                   |                   |  |
| subjects affected / exposed  | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                          | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| polycythaemia vera<br>alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                          | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| prostate cancer<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                   |  |
| subjects affected / exposed <sup>[4]</sup>                               | 26 / 4648 (0.56%) | 28 / 4658 (0.60%) |  |
| occurrences causally related to treatment / all                          | 0 / 26            | 0 / 28            |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| prostate cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[5]</sup> | 0 / 6036 (0.00%) | 1 / 4658 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| prostate cancer recurrent<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[6]</sup>  | 3 / 4648 (0.06%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 3            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| prostate cancer stage ii<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[7]</sup>   | 2 / 4648 (0.04%) | 1 / 4658 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| prostate cancer stage iv<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[8]</sup>   | 0 / 6036 (0.00%) | 1 / 4658 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| prostatic adenoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[9]</sup>          | 1 / 4648 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| rectal adenocarcinoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| rectal cancer<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| rectal cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 1            | 0 / 0            |  |
| rectal cancer stage 0<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| renal cancer<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                         | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| renal cancer recurrent<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 1            | 0 / 0            |  |
| renal cell carcinoma<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |
| subjects affected / exposed   | 5 / 6036 (0.08%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                         | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 1            |  |
| sinonasal papilloma<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| skin cancer<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| small cell lung cancer<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 2            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 1            | 0 / 0            |  |
| small cell lung cancer metastatic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 2            |  |
| spinal cord neoplasm<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| squamous cell carcinoma<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed  | 6 / 6036 (0.10%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 7            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| squamous cell carcinoma of lung<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |
| subjects affected / exposed  | 3 / 6036 (0.05%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 3            | 0 / 3            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 1            | 0 / 2            |  |
| squamous cell carcinoma of skin<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 5 / 6036 (0.08%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| squamous cell carcinoma of the tongue           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| squamous cell carcinoma of the oral cavity      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| squamous cell carcinoma of the vulva            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| t-cell lymphoma                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| testicular neoplasm                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[10]</sup>     | 1 / 4648 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| testicular seminoma (pure)                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed <sup>[11]</sup>     | 0 / 6036 (0.00%) | 1 / 4658 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| throat cancer                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| thymoma malignant                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| thyroid cancer                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| thyroid neoplasm                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tongue carcinoma stage iv                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (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     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tonsil cancer                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tonsil cancer metastatic                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| transitional cell carcinoma                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| transitional cell carcinoma recurrent           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ureteric cancer                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| uterine cancer                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[12]</sup>     | 0 / 6036 (0.00%) | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |

|   |                                      |                                      |  |
|---|--------------------------------------|--------------------------------------|--|
| uterine leiomyoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[13]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all              | 1 / 1388 (0.07%)<br>0 / 1<br>0 / 0   | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0   |  |
| uterine neoplasm<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[14]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all               | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0   | 1 / 1394 (0.07%)<br>0 / 1<br>0 / 0   |  |
| Vascular disorders<br>accelerated hypertension<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 2 / 6036 (0.03%)<br>0 / 2<br>0 / 0   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0   |  |
| aneurysm<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                       | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0   |  |
| aortic aneurysm<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                | 18 / 6036 (0.30%)<br>0 / 18<br>0 / 0 | 14 / 6052 (0.23%)<br>0 / 14<br>0 / 0 |  |
| aortic aneurysm rupture<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                        | 3 / 6036 (0.05%)<br>0 / 3<br>0 / 1   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 1   |  |
| aortic dissection<br>alternative dictionary used:<br>MedDRA 15.1  |                                      |                                      |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| aortic occlusion                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| aortic elongation                               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| aortic rupture                                  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| aortic stenosis                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 18 / 6036 (0.30%) | 17 / 6052 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 18            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| aortitis  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| arterial haemorrhage                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| arterial disorder                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arterial insufficiency                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arterial occlusive disease                         |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arterial perforation                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arterial stenosis                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arterial thrombosis                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arteriosclerosis                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| artery dissection                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| axillary vein thrombosis                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| blood pressure inadequately controlled          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| brachiocephalic artery stenosis                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| circulatory collapse                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| deep vein thrombosis                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 11 / 6036 (0.18%) | 16 / 6052 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 1 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| dry gangrene                                    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| embolism arterial                               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| extremity necrosis                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| femoral artery aneurysm                         |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| femoral artery occlusion                        |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%)  | 7 / 6052 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| femoral artery perforation                      |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| haematoma  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 7 / 6036 (0.12%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 7             | 0 / 3             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| haemorrhage  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 3             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypertension                                       |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 21 / 6036 (0.35%) | 18 / 6052 (0.30%) |  |
| occurrences causally related to<br>treatment / all | 1 / 23            | 2 / 19            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypertensive crisis                                |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 9 / 6036 (0.15%)  | 14 / 6052 (0.23%) |  |
| occurrences causally related to<br>treatment / all | 1 / 9             | 0 / 16            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypertensive emergency                             |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 3             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypotension  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 11 / 6036 (0.18%) | 17 / 6052 (0.28%) |  |
| occurrences causally related to<br>treatment / all | 0 / 12            | 0 / 18            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypovolaemic shock                                 |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| iliac artery occlusion                          |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| iliac artery rupture                            |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| intermittent claudication                       |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 16 / 6052 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 1 / 20            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| jugular vein thrombosis                         |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| lymphatic fistula                               |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| lymphorrhoea                                    |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |

|  |                                      |                                      |  |  |
|--|--------------------------------------|--------------------------------------|--|--|
| malignant hypertension<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                | 4 / 6036 (0.07%)<br>0 / 4<br>0 / 0   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0   |  |  |
| orthostatic hypotension<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all               | 11 / 6036 (0.18%)<br>1 / 11<br>0 / 0 | 4 / 6052 (0.07%)<br>0 / 4<br>0 / 0   |  |  |
| peripheral arterial occlusive disease<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 52 / 6036 (0.86%)<br>0 / 66<br>0 / 1 | 50 / 6052 (0.83%)<br>1 / 66<br>0 / 0 |  |  |
| peripheral artery aneurysm<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all            | 2 / 6036 (0.03%)<br>0 / 2<br>0 / 0   | 2 / 6052 (0.03%)<br>0 / 2<br>0 / 0   |  |  |
| peripheral artery stenosis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all            | 19 / 6036 (0.31%)<br>0 / 21<br>0 / 0 | 10 / 6052 (0.17%)<br>0 / 10<br>0 / 0 |  |  |
| peripheral artery thrombosis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0   | 6 / 6052 (0.10%)<br>0 / 7<br>0 / 0   |  |  |
| peripheral embolism<br>alternative dictionary used:<br>MedDRA 15.1   |                                      |                                      |  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                             | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |
| peripheral ischaemia<br>alternative dictionary used:<br>MedDRA 15.1         |                   |                   |  |
| subjects affected / exposed   | 12 / 6036 (0.20%) | 20 / 6052 (0.33%) |  |
| occurrences causally related to treatment / all                             | 0 / 14            | 0 / 25            |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 1             |  |
| peripheral vascular disorder<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 21 / 6036 (0.35%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all                             | 0 / 25            | 0 / 11            |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |
| shock<br>alternative dictionary used:<br>MedDRA 15.1                        |                   |                   |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                             | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 1             |  |
| shock haemorrhagic<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                             | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all                                  | 0 / 1             | 0 / 0             |  |
| subclavian artery occlusion<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                   |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                             | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |
| subclavian artery stenosis<br>alternative dictionary used:<br>MedDRA 15.1   |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 4 / 6052 (0.07%)  |  |
| occurrences causally related to treatment / all                             | 0 / 3             | 0 / 4             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subclavian artery thrombosis<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                          | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |
| temporal arteritis<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                          | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |
| thrombophlebitis<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                          | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |
| thrombophlebitis superficial<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                          | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |
| thrombosis<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                          | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |
| varicose vein<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all                          | 0 / 2            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |
| vascular occlusion<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vasculitis                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vena cava thrombosis                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| venous thrombosis                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| venous thrombosis limb                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Surgical and medical procedures                 |                  |                  |  |
| abdominal hernia repair                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| adrenalectomy                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| amputation                                      |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| analgesic therapy                               |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| aneurysm repair                                 |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| angioplasty                                     |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 12 / 6036 (0.20%) | 8 / 6052 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| ankle arthroplasty                              |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| aortic aneurysm repair                          |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |

|  |                                    |                                    |  |  |
|--|------------------------------------|------------------------------------|--|--|
| aortic bypass<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all               | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| aortic valve repair<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all         | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| aortic valve replacement<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | 4 / 6036 (0.07%)<br>0 / 4<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| arterial stent insertion<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| atherectomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                 | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| atrial septal defect repair<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| autonomic nerve operation<br>alternative dictionary used:<br>MedDRA 15.1   |                                    |                                    |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bladder neck suspension                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[15]</sup>     | 1 / 1388 (0.07%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bone operation                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bronchial lesion excision                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cancer surgery                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cardiac ablation                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cardiac pacemaker battery replacement           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                                  | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| cardiac pacemaker insertion<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |
| subjects affected / exposed  | 6 / 6036 (0.10%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                                  | 0 / 6            | 0 / 4            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| cardiac pacemaker replacement<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                  | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| cardiac rehabilitation therapy<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                                  | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| cardiac resynchronisation therapy<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                  | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| cardioversion<br>alternative dictionary used:<br>MedDRA 15.1                     |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                  | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| carotid angioplasty<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                  | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
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| carotid endarterectomy                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| carotid revascularisation                          |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| carpal tunnel decompression                        |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| catheter placement                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| cataract operation                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| cholecystectomy                                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 5            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| colectomy  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 4 / 6036 (0.07%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| colostomy closure                               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| coronary angioplasty                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 13 / 6036 (0.22%) | 21 / 6052 (0.35%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| coronary arterial stent insertion               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 11 / 6036 (0.18%) | 12 / 6052 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| coronary artery bypass                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 54 / 6036 (0.89%) | 59 / 6052 (0.97%) |  |
| occurrences causally related to treatment / all | 0 / 54            | 0 / 59            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| coronary revascularisation                      |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 82 / 6036 (1.36%) | 79 / 6052 (1.31%) |  |
| occurrences causally related to treatment / all | 0 / 92            | 0 / 89            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cox-maze procedure                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| debridement  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| diaphragmatic operation                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| elective surgery                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| endarterectomy                                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| endovenous ablation                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| exploratory operation                              |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| explorative laparotomy                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| eye operation                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| foot amputation                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| gastrectomy                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| gastric bypass                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| gastrointestinal endoscopic therapy             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| haematoma evacuation                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                   |                  |  |  |
|--|-------------------|------------------|--|--|
| heart valve replacement<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 0             | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0             | 0 / 0            |  |  |
| hernia repair<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1             | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0             | 0 / 0            |  |  |
| hip arthroplasty<br>alternative dictionary used:<br>MedDRA 15.1        |                   |                  |  |  |
| subjects affected / exposed  | 11 / 6036 (0.18%) | 7 / 6052 (0.12%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 12            | 0 / 7            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0             | 0 / 0            |  |  |
| high frequency ablation<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 0             | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0             | 0 / 0            |  |  |
| hip surgery<br>alternative dictionary used:<br>MedDRA 15.1             |                   |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1             | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0             | 0 / 0            |  |  |
| hospitalisation<br>alternative dictionary used:<br>MedDRA 15.1         |                   |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1             | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0             | 0 / 0            |  |  |
| hysterectomy<br>alternative dictionary used:<br>MedDRA 15.1            |                   |                  |  |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| subjects affected / exposed <sup>[16]</sup>  | 1 / 1388 (0.07%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all                                      | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| implantable defibrillator insertion<br>alternative dictionary used:<br>MedDRA 15.1   |                   |                   |  |
| subjects affected / exposed  | 11 / 6036 (0.18%) | 13 / 6052 (0.21%) |  |
| occurrences causally related to treatment / all                                      | 0 / 11            | 0 / 13            |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| implantable defibrillator replacement<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                      | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| incisional drainage<br>alternative dictionary used:<br>MedDRA 15.1                   |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                                      | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| incisional hernia repair<br>alternative dictionary used:<br>MedDRA 15.1              |                   |                   |  |
| subjects affected / exposed  | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                                      | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| inguinal hernia repair<br>alternative dictionary used:<br>MedDRA 15.1                |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 5 / 6052 (0.08%)  |  |
| occurrences causally related to treatment / all                                      | 0 / 1             | 0 / 5             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| intervertebral disc operation<br>alternative dictionary used:<br>MedDRA 15.1         |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                                      | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| intraocular lens implant<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all                      | 0 / 3             | 0 / 1             |  |
| deaths causally related to<br>treatment / all                           | 0 / 0             | 0 / 0             |  |
| joint arthroplasty<br>alternative dictionary used:<br>MedDRA 15.1       |                   |                   |  |
| subjects affected / exposed   | 3 / 6036 (0.05%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all                      | 0 / 3             | 0 / 1             |  |
| deaths causally related to<br>treatment / all                           | 0 / 0             | 0 / 0             |  |
| knee arthroplasty<br>alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed   | 12 / 6036 (0.20%) | 12 / 6052 (0.20%) |  |
| occurrences causally related to<br>treatment / all                      | 0 / 14            | 0 / 12            |  |
| deaths causally related to<br>treatment / all                           | 0 / 0             | 0 / 0             |  |
| knee operation<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all                      | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all                           | 0 / 0             | 0 / 0             |  |
| leg amputation<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                   |  |
| subjects affected / exposed   | 5 / 6036 (0.08%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all                      | 0 / 6             | 0 / 3             |  |
| deaths causally related to<br>treatment / all                           | 0 / 0             | 0 / 0             |  |
| lens extraction<br>alternative dictionary used:<br>MedDRA 15.1          |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all                      | 0 / 2             | 0 / 1             |  |
| deaths causally related to<br>treatment / all                           | 0 / 0             | 0 / 0             |  |
| lipoma excision<br>alternative dictionary used:<br>MedDRA 15.1          |                   |                   |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| mastectomy                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| medical device change                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| medical device removal                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| mitral valve replacement                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| nephrectomy                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| open reduction of fracture                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                    |                    |  |  |
|--|--------------------|--------------------|--|--|
| osteosynthesis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                     | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0              | 0 / 1              |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0              | 0 / 0              |  |  |
| osteotomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                          | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0              | 0 / 1              |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0              | 0 / 0              |  |  |
| pancreatectomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                     | 1 / 6036 (0.02%)   | 0 / 6052 (0.00%)   |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1              | 0 / 0              |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0              | 0 / 0              |  |  |
| pancreaticoduodenectomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed            | 0 / 6036 (0.00%)   | 2 / 6052 (0.03%)   |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0              | 0 / 2              |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0              | 0 / 0              |  |  |
| penile repair<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[17]</sup>      | 0 / 6036 (0.00%)   | 1 / 4658 (0.02%)   |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0              | 0 / 1              |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0              | 0 / 0              |  |  |
| percutaneous coronary intervention<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 192 / 6036 (3.18%) | 182 / 6052 (3.01%) |  |  |
| occurrences causally related to<br>treatment / all   | 1 / 217            | 1 / 214            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0              | 0 / 0              |  |  |
| peripheral artery angioplasty<br>alternative dictionary used:<br>MedDRA 15.1                                     |                    |                    |  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 3 / 6036 (0.05%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all                                  | 0 / 5            | 0 / 5            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| peripheral artery bypass<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |
| subjects affected / exposed  | 5 / 6036 (0.08%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all                                  | 1 / 5            | 0 / 6            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| peripheral artery stent insertion<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                  | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| peripheral endarterectomy<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed  | 3 / 6036 (0.05%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all                                  | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| peripheral nerve transposition<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                  | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| peripheral revascularisation<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                  | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |
| prostate ablation<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                  | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                       | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| prostatectomy                                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[18]</sup>        | 0 / 6036 (0.00%) | 2 / 4658 (0.04%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| radioactive iodine therapy                         |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| rectal prolapse repair                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| renal artery angioplasty                           |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| renal sympathetic nerve ablation                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| resection of rectum                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| resuscitation                                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| retinopexy                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| rotator cuff repair                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| shoulder arthroplasty                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| shoulder operation                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| skin neoplasm excision                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| spinal decompression                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| spinal fusion surgery<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 5 / 6036 (0.08%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 5            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| spinal laminectomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed    | 4 / 6036 (0.07%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 4            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| spinal operation<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed      | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| stent placement<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed       | 3 / 6036 (0.05%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 3            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| sympathectomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed         | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| tenotomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed              | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| therapeutic embolisation<br>alternative dictionary used:<br>MedDRA 15.1                             |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| therapy cessation                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| thrombectomy                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| thrombosis prophylaxis                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| thyroidectomy                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| toe amputation                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tongue operation                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| total adrenalectomy                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| transmyocardial revascularisation                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| transurethral bladder resection                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| transurethral prostatectomy                        |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[19]</sup>        | 2 / 4648 (0.04%) | 1 / 4658 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| tricuspid valve repair                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| tumour excision                                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| ureteral stent insertion                           |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ureteral stent removal                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vaginal prolapse repair                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[20]</sup>     | 1 / 1388 (0.07%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| valvuloplasty cardiac                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vascular graft                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| venous stent insertion                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ventricular assist device insertion             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                                    |                                    |  |
|--|------------------------------------|------------------------------------|--|
| vitrectomy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 2 / 6052 (0.03%)<br>0 / 2<br>0 / 0 |  |
| wound drainage<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Pregnancy, puerperium and perinatal<br>conditions<br>abortion spontaneous<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[21]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 1394 (0.07%)<br>0 / 1<br>0 / 0 |  |
| pregnancy<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[22]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 1394 (0.07%)<br>0 / 1<br>0 / 0 |  |
| General disorders and administration<br>site conditions<br>adverse drug reaction<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |
| asthenia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 5 / 6036 (0.08%)<br>0 / 5<br>0 / 0 | 9 / 6052 (0.15%)<br>2 / 9<br>0 / 0 |  |
| cardiac death  |                                    |                                    |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 5 / 6052 (0.08%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 5             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 5             |  |
| chest discomfort                                   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 7 / 6036 (0.12%)  | 12 / 6052 (0.20%) |  |
| occurrences causally related to<br>treatment / all | 0 / 7             | 2 / 13            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| chest pain   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 37 / 6036 (0.61%) | 34 / 6052 (0.56%) |  |
| occurrences causally related to<br>treatment / all | 3 / 38            | 0 / 42            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| death  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 20 / 6036 (0.33%) | 14 / 6052 (0.23%) |  |
| occurrences causally related to<br>treatment / all | 2 / 20            | 0 / 14            |  |
| deaths causally related to<br>treatment / all      | 2 / 20            | 0 / 14            |  |
| device breakage                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| device dislocation                                 |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 5             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| device end of service                              |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| device inappropriate shock delivery<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| device failure<br>alternative dictionary used:<br>MedDRA 15.1                      |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                    | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| device malfunction<br>alternative dictionary used:<br>MedDRA 15.1                  |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 6            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| device material issue<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| device occlusion<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                    | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| drowning<br>alternative dictionary used:<br>MedDRA 15.1                            |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 1            |  |

|  |                  |                  |  |  |
|--|------------------|------------------|--|--|
| drug withdrawal syndrome<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| exercise tolerance decreased<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| gait disturbance<br>alternative dictionary used:<br>MedDRA 15.1                      |                  |                  |  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| general physical health deterioration<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| generalised oedema<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |  |
| subjects affected / exposed  | 3 / 6036 (0.05%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 3            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| granuloma<br>alternative dictionary used:<br>MedDRA 15.1                             |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 0            | 1 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| hyperthermia<br>alternative dictionary used:<br>MedDRA 15.1                          |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hypertrophy                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hypothermia                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| impaired healing                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| implant site haematoma                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| incarcerated hernia                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ischaemic ulcer                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                    |                    |  |
|--|--------------------|--------------------|--|
| lead dislodgement                                  |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)   | 2 / 6052 (0.03%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 0              | 0 / 2              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| multi-organ failure                                |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%)   | 6 / 6052 (0.10%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 4              | 0 / 6              |  |
| deaths causally related to<br>treatment / all      | 0 / 1              | 0 / 4              |  |
| necrosis   |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)   | 0 / 6052 (0.00%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 2              | 0 / 0              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| necrobiosis  |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| non-cardiac chest pain                             |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 107 / 6036 (1.77%) | 108 / 6052 (1.78%) |  |
| occurrences causally related to<br>treatment / all | 1 / 123            | 1 / 118            |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| oedema   |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)   | 0 / 6052 (0.00%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 3              | 0 / 0              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| oedema peripheral                                  |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pain  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pelvic mass                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| peripheral swelling                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| precancerous mucosal lesion                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pyrexia   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| stent-graft endoleak                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |



|  |                   |                   |  |
|--|-------------------|-------------------|--|
| sudden cardiac death                               |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 16 / 6036 (0.27%) | 15 / 6052 (0.25%) |  |
| occurrences causally related to<br>treatment / all | 0 / 16            | 0 / 15            |  |
| deaths causally related to<br>treatment / all      | 0 / 16            | 0 / 15            |  |
| sudden death                                       |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 2             | 0 / 1             |  |
| systemic inflammatory response<br>syndrome         |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 4             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| thrombosis in device                               |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| ulcer haemorrhage                                  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| vascular stent occlusion                           |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| vascular stent restenosis                          |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vascular stent stenosis                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vascular stent thrombosis                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vessel puncture site haematoma                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Immune system disorders                         |                  |                  |  |
| anaphylactic reaction                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| anaphylactic shock                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| drug hypersensitivity                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| hypersensitivity                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Reproductive system and breast disorders        |                   |                   |  |
| amastia   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| benign prostatic hyperplasia                    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed <sup>[23]</sup>     | 10 / 4648 (0.22%) | 12 / 4658 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 1             |  |
| cervical polyp                                  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed <sup>[24]</sup>     | 0 / 6036 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cystocele                                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed <sup>[25]</sup>     | 1 / 1388 (0.07%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| dysmenorrhoea                                   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed <sup>[26]</sup>     | 0 / 6036 (0.00%) | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| menometrorrhagia                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[27]</sup>     | 0 / 6036 (0.00%) | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ovarian cyst                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[28]</sup>     | 2 / 1388 (0.14%) | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| penile necrosis                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[29]</sup>     | 0 / 6036 (0.00%) | 1 / 4658 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| peyronie's disease                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[30]</sup>     | 1 / 4648 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| prostatitis                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[31]</sup>     | 4 / 4648 (0.09%) | 2 / 4658 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| rectocele                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[32]</sup>     | 0 / 6036 (0.00%) | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                                      |                                      |  |
|--|--------------------------------------|--------------------------------------|--|
| testicular disorder<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[33]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                       | 1 / 4648 (0.02%)<br>0 / 1<br>0 / 0   | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0   |  |
| uterine polyp<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[34]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 1388 (0.07%)<br>0 / 1<br>0 / 0   | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0   |  |
| uterine prolapse<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[35]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 2 / 1388 (0.14%)<br>0 / 2<br>0 / 0   | 2 / 1394 (0.14%)<br>0 / 2<br>0 / 0   |  |
| Respiratory, thoracic and mediastinal disorders<br>acute pulmonary oedema<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 8 / 6036 (0.13%)<br>0 / 10<br>0 / 1  | 5 / 6052 (0.08%)<br>0 / 5<br>0 / 0   |  |
| acute respiratory distress syndrome<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                       | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 1   | 2 / 6052 (0.03%)<br>0 / 2<br>0 / 1   |  |
| acute respiratory failure<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 14 / 6036 (0.23%)<br>0 / 16<br>0 / 1 | 20 / 6052 (0.33%)<br>0 / 20<br>0 / 3 |  |
| alveolitis<br>alternative dictionary used:<br>MedDRA 15.1  |                                      |                                      |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| aspiration                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| asphyxia  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| asthma  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 8 / 6036 (0.13%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| atelectasis                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bronchiectasis                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bronchitis chronic                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| bronchospasm                                       |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| chronic obstructive pulmonary<br>disease           |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 43 / 6036 (0.71%) | 47 / 6052 (0.78%) |  |
| occurrences causally related to<br>treatment / all | 0 / 55            | 0 / 55            |  |
| deaths causally related to<br>treatment / all      | 0 / 1             | 0 / 3             |  |
| chylothorax  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| cough  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| dyspnoea   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 26 / 6036 (0.43%) | 23 / 6052 (0.38%) |  |
| occurrences causally related to<br>treatment / all | 0 / 29            | 0 / 23            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| dyspnoea exertional                                |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 6 / 6036 (0.10%)  | 10 / 6052 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 6             | 0 / 10            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| emphysema  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| epistaxis                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| haemoptysis                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 11           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| haemothorax                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hiccups   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hydrothorax                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hypercapnia                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |



|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| hypoxia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                       | 7 / 6036 (0.12%) | 4 / 6052 (0.07%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 7            | 0 / 4            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| idiopathic pulmonary fibrosis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |  |
| interstitial lung disease<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed     | 4 / 6036 (0.07%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 1 / 4            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| lung consolidation<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed            | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| lung infiltration<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed             | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| mediastinal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed       | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| nasal septum deviation<br>alternative dictionary used:<br>MedDRA 15.1                                       |                  |                  |  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| organising pneumonia                            |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 1 / 2            | 1 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| pickwickian syndrome                            |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| pleural effusion                                |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 8 / 6036 (0.13%) | 12 / 6052 (0.20%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1             |  |
| pleurisy  |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| pleuritic pain                                  |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| pneumomediastinum                               |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| pneumonia aspiration<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed  | 7 / 6036 (0.12%) | 8 / 6052 (0.13%) |  |
| occurrences causally related to<br>treatment / all                             | 0 / 8            | 0 / 11           |  |
| deaths causally related to<br>treatment / all                                  | 0 / 3            | 0 / 0            |  |
| pneumonitis<br>alternative dictionary used:<br>MedDRA 15.1                     |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                             | 1 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                                  | 0 / 0            | 0 / 0            |  |
| pneumothorax<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all                             | 0 / 3            | 0 / 3            |  |
| deaths causally related to<br>treatment / all                                  | 0 / 0            | 0 / 0            |  |
| pneumothorax spontaneous<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                             | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                  | 0 / 0            | 0 / 0            |  |
| pulmonary alveolar haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                             | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                  | 0 / 0            | 0 / 0            |  |
| pulmonary arterial hypertension<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                             | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                                  | 0 / 0            | 0 / 0            |  |
| pulmonary congestion<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pulmonary embolism                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 21 / 6036 (0.35%) | 20 / 6052 (0.33%) |  |
| occurrences causally related to treatment / all | 1 / 22            | 1 / 20            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 2             |  |
| pulmonary fibrosis                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%)  | 4 / 6052 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 2             | 0 / 2             |  |
| pulmonary hypertension                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pulmonary infarction                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pulmonary mass                                  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%)  | 5 / 6052 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| pulmonary oedema                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 8 / 6036 (0.13%)  | 8 / 6052 (0.13%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| respiratory arrest<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                          | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2             | 0 / 2             |  |
| deaths causally related to<br>treatment / all   | 0 / 1             | 0 / 0             |  |
| respiratory distress<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                        | 2 / 6036 (0.03%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2             | 0 / 3             |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |
| respiratory failure<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                         | 17 / 6036 (0.28%) | 16 / 6052 (0.26%) |  |
| occurrences causally related to<br>treatment / all  | 0 / 17            | 0 / 17            |  |
| deaths causally related to<br>treatment / all   | 0 / 4             | 0 / 5             |  |
| sleep apnoea syndrome<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                       | 3 / 6036 (0.05%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all  | 0 / 3             | 0 / 3             |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |
| tracheomalacia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                              | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |
| Psychiatric disorders<br>abnormal behaviour<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |
| acute psychosis<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                                       | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                        | 0 / 0            | 0 / 0            |  |
| acute stress disorder   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1                          |                  |                  |  |
| subjects affected / exposed                                       | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                        | 0 / 0            | 0 / 0            |  |
| adjustment disorder   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1                          |                  |                  |  |
| subjects affected / exposed                                       | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                   | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                        | 0 / 0            | 0 / 0            |  |
| adjustment disorder with anxiety                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1                          |                  |                  |  |
| subjects affected / exposed                                       | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                        | 0 / 0            | 0 / 0            |  |
| adjustment disorder with depressed mood                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1                          |                  |                  |  |
| subjects affected / exposed                                       | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                        | 0 / 0            | 0 / 0            |  |
| adjustment disorder with mixed disturbance of emotion and conduct |                  |                  |  |
| alternative dictionary used: MedDRA 15.1                          |                  |                  |  |
| subjects affected / exposed                                       | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                        | 0 / 0            | 0 / 0            |  |
| aggression  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1                          |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| alcohol abuse                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| alcohol withdrawal syndrome                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| alcoholism                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| anxiety   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| anxiety disorder                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| completed suicide                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 1            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| confusional state                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| delirium   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| delirium tremens                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| depression   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| depression suicidal                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| generalised anxiety disorder                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| hallucination                                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| hypomania                                       |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| major depression                                |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| mental disorder                                 |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| mental status changes                           |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 13 / 6052 (0.21%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| panic attack                                    |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| post-traumatic stress disorder                  |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |

|  |                                    |                                    |  |
|--|------------------------------------|------------------------------------|--|
| psychogenic seizure<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                             | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |
| psychotic disorder<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                              | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 2 / 6052 (0.03%)<br>0 / 2<br>0 / 0 |  |
| suicidal ideation<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                               | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |
| suicide attempt<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                 | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |
| Hepatobiliary disorders<br>autoimmune hepatitis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 6036 (0.02%)<br>1 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |
| bile duct obstruction<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                           | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 1 |  |
| bile duct stenosis<br>alternative dictionary used:<br>MedDRA 15.1  |                                    |                                    |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| bile duct stone                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%)  | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| biliary colic                                   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| biliary tract disorder                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cholangitis acute                               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cholangitis                                     |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 4 / 6052 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cholecystitis                                   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 19 / 6036 (0.31%) | 16 / 6052 (0.26%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 1 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|   |                   |                   |  |  |
|---|-------------------|-------------------|--|--|
| cholecystitis acute<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed   | 12 / 6036 (0.20%) | 15 / 6052 (0.25%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 12            | 0 / 16            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |  |
| cholecystitis chronic<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 4 / 6036 (0.07%)  | 1 / 6052 (0.02%)  |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 4             | 0 / 1             |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |  |
| cholelithiasis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed        | 23 / 6036 (0.38%) | 22 / 6052 (0.36%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 23            | 1 / 23            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |  |
| cholestasis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed           | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0             | 0 / 1             |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |  |
| gallbladder disorder<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1             | 0 / 0             |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 0             |  |  |
| hepatic cirrhosis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed     | 2 / 6036 (0.03%)  | 3 / 6052 (0.05%)  |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2             | 0 / 3             |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0             | 0 / 1             |  |  |
| hepatic lesion<br>alternative dictionary used:<br>MedDRA 15.1                                       |                   |                   |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hepatic steatosis                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hepatitis alcoholic                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hepatomegaly                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hydrocholecystis                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ischaemic hepatitis                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| jaundice  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| jaundice cholestatic<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                                 | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |
| jaundice extrahepatic obstructive<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                    | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |
| liver disorder<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                                       | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |
| liver injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |
| portal vein thrombosis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                               | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |
| Investigations<br>alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all   | 1 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |
| angiogram<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 6036 (0.12%)  | 7 / 6052 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| anticoagulation drug level above therapeutic    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| arteriogram                                     |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| arteriogram coronary                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 16 / 6036 (0.27%) | 17 / 6052 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 16            | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| arteriogram renal                               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| aspartate aminotransferase increased            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| biopsy brain                                    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| blood creatine phosphokinase increased          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| blood creatinine increased                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| blood glucose decreased                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| blood glucose increased                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| blood osmolarity decreased                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| blood pressure increased                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cardiac function test                           |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cardiac stress test abnormal                    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cardiovascular evaluation                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cardiovascular examination                      |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| carotid bruit                                   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| catheterisation cardiac                         |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 10 / 6036 (0.17%) | 14 / 6052 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| clostridium test positive<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |  |
| colonoscopy<br>alternative dictionary used:<br>MedDRA 15.1                  |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 1            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |  |
| computerised tomogram<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |  |
| computerised tomogram thorax<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |  |
| diagnostic procedure<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |  |
| ejection fraction decreased<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |  |
| subjects affected / exposed   | 5 / 6036 (0.08%) | 4 / 6052 (0.07%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 5            | 0 / 4            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0            | 0 / 0            |  |  |
| electrocardiogram abnormal<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| electrocardiogram qt prolonged<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| endoscopy gastrointestinal<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| gamma-glutamyltransferase increased<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                    | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| haemoglobin decreased<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| heart rate irregular<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| hepatic enzyme increased<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| international normalised ratio decreased        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| international normalised ratio increased        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| investigation                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| liver function test abnormal                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| myocardial necrosis marker increased            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| oesophagogastroduodenoscopy                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| peripheral arteriogram                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| prostatic specific antigen increased            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[36]</sup>     | 2 / 4648 (0.04%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| transaminases increased                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| troponin increased                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ureteroscopy                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vitamin b12 decreased                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                                    |                                    |  |
|--|------------------------------------|------------------------------------|--|
| weight decreased<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 1 / 6036 (0.02%)<br>1 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Injury, poisoning and procedural<br>complications<br>abdominal wound dehiscence<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |
| accident<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 2 / 6036 (0.03%)<br>0 / 2<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |
| accidental exposure to product<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |
| acetabulum fracture<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |
| accidental overdose<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |
| alcohol poisoning<br>alternative dictionary used:<br>MedDRA 15.1   |                                    |                                    |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| anaemia postoperative                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| anal injury                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| anastomotic stenosis                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| anastomotic ulcer haemorrhage                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ankle fracture                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 9 / 6036 (0.15%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| back injury                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| brain contusion<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed             | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cartilage injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed            | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cervical vertebral fracture<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| chemical burn of skin<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed       | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| chemical injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed             | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| chest injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| clavicle fracture<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| colon injury                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| compression fracture                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| concussion                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| contrast media reaction                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| contusion                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| coronary artery restenosis                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| craniocerebral injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| crush injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed          | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cystitis radiation<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed    | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| extradural haematoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| eye injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed            | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| facial bones fracture<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 3 / 6036 (0.05%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 3            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| fall<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 39 / 6036 (0.65%) | 50 / 6052 (0.83%) |  |
| occurrences causally related to treatment / all | 0 / 40            | 0 / 53            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| femur fracture                                  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%)  | 6 / 6052 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| femoral neck fracture                           |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 6 / 6052 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| fibula fracture                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| foot fracture                                   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| foreign body                                    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| fracture  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| fractured sacrum                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| gastrointestinal anastomotic<br>complication       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| gastrointestinal injury                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| gastrointestinal stoma complication                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| graft thrombosis                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| gun shot wound                                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 1            | 0 / 1            |  |
| hand fracture                                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| head injury                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| heat illness                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hip fracture                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| humerus fracture                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| incisional hernia                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| injury  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |  |
|--|------------------|------------------|--|--|
| intentional overdose                               |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| jaw fracture                                       |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| joint injury                                       |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| joint dislocation                                  |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 5 / 6036 (0.08%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 6            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| laceration   |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| ligament injury                                    |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| ligament sprain                                    |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| limb traumatic amputation<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| lower limb fracture<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |
| subjects affected / exposed  | 4 / 6036 (0.07%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                          | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| lumbar vertebral fracture<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| meniscus injury<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all                          | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| multiple fractures<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| multiple injuries<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 1            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| muscle contusion<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                      | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                           | 0 / 0            | 0 / 0            |  |
| muscle rupture<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all                      | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                           | 0 / 0            | 0 / 0            |  |
| muscle injury<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                      | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                           | 0 / 0            | 0 / 0            |  |
| nerve root injury lumbar<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                      | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                           | 0 / 0            | 0 / 0            |  |
| overdose<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                      | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                           | 0 / 0            | 0 / 0            |  |
| patella fracture<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                      | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                           | 0 / 0            | 0 / 0            |  |
| pelvic fracture<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| peripheral arterial reocclusion<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| peripheral artery restenosis<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| periprosthetic fracture<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| poisoning<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| post concussion syndrome<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| post laminectomy syndrome<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |  |
|--|------------------|------------------|--|--|
| post procedural bile leak<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| post procedural complication<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| post procedural haematoma<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| post procedural haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |  |
| subjects affected / exposed  | 4 / 6036 (0.07%) | 4 / 6052 (0.07%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 4            | 0 / 4            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| post procedural myocardial infarction<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 5 / 6036 (0.08%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 6            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| post procedural stroke<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                   | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| postoperative fever<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| postoperative ileus                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| postoperative respiratory failure               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| postoperative thoracic procedure complication   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| postoperative wound complication                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| procedural haemorrhage                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| procedural hypotension                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pubis fracture                                  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pulmonary contusion                             |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| radius fracture                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| rib fracture                                    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%)  | 8 / 6052 (0.13%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| road traffic accident                           |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 15 / 6036 (0.25%) | 15 / 6052 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 3             | 0 / 4             |  |
| seroma  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| skull fracture<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed              | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |  |
| soft tissue injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed          | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 1 / 2            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| spinal compression fracture<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 3 / 6036 (0.05%) | 5 / 6052 (0.08%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 3            | 0 / 5            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| spinal cord injury<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed          | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| spinal cord injury cervical<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| spinal fracture<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed             | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| splenic rupture<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| sternal fracture                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| stoma site haemorrhage                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| subdural haematoma                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 1 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| subdural haemorrhage                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| tendon injury                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tendon rupture                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 8 / 6036 (0.13%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 9            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| thermal burn                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| thoracic vertebral fracture                        |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| tibia fracture                                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 5 / 6036 (0.08%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to<br>treatment / all | 0 / 5            | 0 / 4            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| tooth fracture                                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| toxicity to various agents                         |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 4            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 1            |  |
| traumatic amputation                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| traumatic fracture                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| traumatic haematoma                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| traumatic intracranial haemorrhage              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| traumatic liver injury                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ulna fracture                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| upper limb fracture                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vascular graft occlusion                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| vascular graft thrombosis<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0            | 0 / 0            |  |
| vascular pseudoaneurysm<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all                              | 0 / 3            | 0 / 3            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0            | 0 / 0            |  |
| vascular pseudoaneurysm ruptured<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0            | 0 / 1            |  |
| wound<br>alternative dictionary used:<br>MedDRA 15.1                            |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0            | 0 / 3            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0            | 0 / 0            |  |
| wound complication<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0            | 0 / 0            |  |
| wound dehiscence<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                              | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0            | 0 / 0            |  |
| wound haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| wrist fracture                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Congenital, familial and genetic disorders      |                  |                  |  |
| arteriovenous malformation                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| atrial septal defect                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| dermoid cyst                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hydrocele                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed <sup>[37]</sup>     | 0 / 6036 (0.00%) | 2 / 4658 (0.04%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hypertrophic cardiomyopathy                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                    |                    |  |
|---|--------------------|--------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| leukodystrophy                                  |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| phimosi   |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed <sup>[38]</sup>     | 0 / 6036 (0.00%)   | 1 / 4658 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| Cardiac disorders                               |                    |                    |  |
| acute coronary syndrome                         |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 9 / 6036 (0.15%)   | 4 / 6052 (0.07%)   |  |
| occurrences causally related to treatment / all | 0 / 9              | 1 / 4              |  |
| deaths causally related to treatment / all      | 0 / 1              | 0 / 1              |  |
| acute myocardial infarction                     |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 146 / 6036 (2.42%) | 137 / 6052 (2.26%) |  |
| occurrences causally related to treatment / all | 5 / 168            | 4 / 149            |  |
| deaths causally related to treatment / all      | 0 / 16             | 0 / 4              |  |
| adams-stokes syndrome                           |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)   | 0 / 6052 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1              | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| angina pectoris                                 |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |

|   |                    |                    |  |
|---|--------------------|--------------------|--|
| subjects affected / exposed                     | 102 / 6036 (1.69%) | 98 / 6052 (1.62%)  |  |
| occurrences causally related to treatment / all | 3 / 113            | 3 / 103            |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| angina unstable                                 |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 298 / 6036 (4.94%) | 289 / 6052 (4.78%) |  |
| occurrences causally related to treatment / all | 7 / 389            | 6 / 363            |  |
| deaths causally related to treatment / all      | 0 / 2              | 0 / 0              |  |
| aortic valve disease                            |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%)   | 1 / 6052 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 4              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 1              |  |
| aortic valve incompetence                       |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)   | 2 / 6052 (0.03%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 2              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| aortic valve sclerosis                          |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 0              |  |
| aortic valve stenosis                           |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%)   | 6 / 6052 (0.10%)   |  |
| occurrences causally related to treatment / all | 0 / 7              | 0 / 8              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 1              |  |
| arrhythmia                                      |                    |                    |  |
| alternative dictionary used: MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%)   | 3 / 6052 (0.05%)   |  |
| occurrences causally related to treatment / all | 0 / 5              | 0 / 3              |  |
| deaths causally related to treatment / all      | 0 / 0              | 0 / 2              |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| arteriosclerosis coronary artery<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 3             | 0 / 1             |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0             | 0 / 0             |  |
| arteriospasm coronary<br>alternative dictionary used:<br>MedDRA 15.1            |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 1             | 0 / 2             |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0             | 0 / 0             |  |
| atrial flutter<br>alternative dictionary used:<br>MedDRA 15.1                   |                   |                   |  |
| subjects affected / exposed   | 25 / 6036 (0.41%) | 16 / 6052 (0.26%) |  |
| occurrences causally related to<br>treatment / all                              | 0 / 27            | 1 / 18            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0             | 0 / 0             |  |
| atrial fibrillation<br>alternative dictionary used:<br>MedDRA 15.1              |                   |                   |  |
| subjects affected / exposed   | 86 / 6036 (1.42%) | 78 / 6052 (1.29%) |  |
| occurrences causally related to<br>treatment / all                              | 1 / 109           | 2 / 94            |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0             | 0 / 0             |  |
| atrial tachycardia<br>alternative dictionary used:<br>MedDRA 15.1               |                   |                   |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0             | 0 / 2             |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0             | 0 / 0             |  |
| atrial thrombosis<br>alternative dictionary used:<br>MedDRA 15.1                |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0             | 0 / 0             |  |
| atrioventricular block complete<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 8 / 6036 (0.13%)  | 6 / 6052 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |
| atrioventricular block                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| atrioventricular block second degree            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| bradyarrhythmia                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 5 / 6052 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| bradycardia                                     |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 8 / 6036 (0.13%)  | 11 / 6052 (0.18%) |  |
| occurrences causally related to treatment / all | 0 / 8             | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cardiac arrest                                  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 17 / 6036 (0.28%) | 30 / 6052 (0.50%) |  |
| occurrences causally related to treatment / all | 1 / 18            | 0 / 32            |  |
| deaths causally related to treatment / all      | 1 / 12            | 0 / 21            |  |
| cardiac discomfort                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|   |                   |                    |  |
|---|-------------------|--------------------|--|
| cardiac failure<br>alternative dictionary used:<br>MedDRA 15.1            |                   |                    |  |
| subjects affected / exposed   | 67 / 6036 (1.11%) | 63 / 6052 (1.04%)  |  |
| occurrences causally related to<br>treatment / all                        | 1 / 79            | 1 / 78             |  |
| deaths causally related to<br>treatment / all                             | 0 / 9             | 0 / 8              |  |
| cardiac failure acute<br>alternative dictionary used:<br>MedDRA 15.1      |                   |                    |  |
| subjects affected / exposed   | 11 / 6036 (0.18%) | 9 / 6052 (0.15%)   |  |
| occurrences causally related to<br>treatment / all                        | 0 / 13            | 0 / 9              |  |
| deaths causally related to<br>treatment / all                             | 0 / 1             | 0 / 1              |  |
| cardiac failure chronic<br>alternative dictionary used:<br>MedDRA 15.1    |                   |                    |  |
| subjects affected / exposed   | 7 / 6036 (0.12%)  | 10 / 6052 (0.17%)  |  |
| occurrences causally related to<br>treatment / all                        | 0 / 7             | 0 / 12             |  |
| deaths causally related to<br>treatment / all                             | 0 / 3             | 0 / 4              |  |
| cardiac failure congestive<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                    |  |
| subjects affected / exposed   | 95 / 6036 (1.57%) | 103 / 6052 (1.70%) |  |
| occurrences causally related to<br>treatment / all                        | 1 / 134           | 0 / 138            |  |
| deaths causally related to<br>treatment / all                             | 0 / 4             | 0 / 12             |  |
| cardiac tamponade<br>alternative dictionary used:<br>MedDRA 15.1          |                   |                    |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)   |  |
| occurrences causally related to<br>treatment / all                        | 0 / 2             | 0 / 1              |  |
| deaths causally related to<br>treatment / all                             | 0 / 0             | 0 / 0              |  |
| cardio-respiratory arrest<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                    |  |
| subjects affected / exposed   | 5 / 6036 (0.08%)  | 6 / 6052 (0.10%)   |  |
| occurrences causally related to<br>treatment / all                        | 0 / 5             | 2 / 7              |  |
| deaths causally related to<br>treatment / all                             | 0 / 3             | 1 / 5              |  |
| cardiogenic shock<br>alternative dictionary used:<br>MedDRA 15.1          |                   |                    |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 8 / 6036 (0.13%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all                             | 1 / 8            | 0 / 7            |  |
| deaths causally related to treatment / all                                  | 1 / 4            | 0 / 4            |  |
| cardiopulmonary failure<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                             | 0 / 3            | 0 / 0            |  |
| deaths causally related to treatment / all                                  | 0 / 2            | 0 / 0            |  |
| cardiomyopathy<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all                             | 0 / 1            | 0 / 5            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 2            |  |
| cardiorenal syndrome<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                             | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all                                  | 0 / 1            | 0 / 0            |  |
| cardiovascular insufficiency<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                             | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| chronotropic incompetence<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                             | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| conduction disorder<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |
| subjects affected / exposed   | 4 / 6036 (0.07%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                             | 0 / 4            | 0 / 1            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| congestive cardiomyopathy<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all                        | 0 / 1             | 0 / 2             |  |
| deaths causally related to<br>treatment / all                             | 0 / 0             | 0 / 1             |  |
| coronary artery disease<br>alternative dictionary used:<br>MedDRA 15.1    |                   |                   |  |
| subjects affected / exposed   | 37 / 6036 (0.61%) | 44 / 6052 (0.73%) |  |
| occurrences causally related to<br>treatment / all                        | 1 / 40            | 2 / 45            |  |
| deaths causally related to<br>treatment / all                             | 0 / 3             | 1 / 4             |  |
| coronary artery dissection<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all                        | 0 / 2             | 0 / 0             |  |
| deaths causally related to<br>treatment / all                             | 0 / 0             | 0 / 0             |  |
| coronary artery occlusion<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                   |  |
| subjects affected / exposed   | 3 / 6036 (0.05%)  | 6 / 6052 (0.10%)  |  |
| occurrences causally related to<br>treatment / all                        | 0 / 3             | 0 / 6             |  |
| deaths causally related to<br>treatment / all                             | 0 / 0             | 0 / 0             |  |
| coronary artery stenosis<br>alternative dictionary used:<br>MedDRA 15.1   |                   |                   |  |
| subjects affected / exposed   | 7 / 6036 (0.12%)  | 6 / 6052 (0.10%)  |  |
| occurrences causally related to<br>treatment / all                        | 0 / 7             | 0 / 7             |  |
| deaths causally related to<br>treatment / all                             | 0 / 0             | 0 / 0             |  |
| diastolic dysfunction<br>alternative dictionary used:<br>MedDRA 15.1      |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all                        | 0 / 2             | 0 / 1             |  |
| deaths causally related to<br>treatment / all                             | 0 / 0             | 0 / 0             |  |
| dressler's syndrome<br>alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| extrasystoles                                   |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (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                      |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| intracardiac thrombus                           |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| ischaemic cardiomyopathy                        |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| left ventricular dysfunction                    |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%) | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0             |  |
| left ventricular failure                        |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 4 / 6052 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |

|   |                   |                    |  |
|---|-------------------|--------------------|--|
| microvascular coronary artery disease           |                   |                    |  |
| alternative dictionary used: MedDRA 15.1        |                   |                    |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)   |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| mitral valve incompetence                       |                   |                    |  |
| alternative dictionary used: MedDRA 15.1        |                   |                    |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%)  | 4 / 6052 (0.07%)   |  |
| occurrences causally related to treatment / all | 0 / 4             | 0 / 6              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| mitral valve stenosis                           |                   |                    |  |
| alternative dictionary used: MedDRA 15.1        |                   |                    |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)   |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0              |  |
| myocardial infarction                           |                   |                    |  |
| alternative dictionary used: MedDRA 15.1        |                   |                    |  |
| subjects affected / exposed                     | 82 / 6036 (1.36%) | 100 / 6052 (1.65%) |  |
| occurrences causally related to treatment / all | 1 / 88            | 0 / 107            |  |
| deaths causally related to treatment / all      | 0 / 14            | 0 / 17             |  |
| myocardial ischaemia                            |                   |                    |  |
| alternative dictionary used: MedDRA 15.1        |                   |                    |  |
| subjects affected / exposed                     | 15 / 6036 (0.25%) | 9 / 6052 (0.15%)   |  |
| occurrences causally related to treatment / all | 1 / 16            | 1 / 9              |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 3              |  |
| myocardial rupture                              |                   |                    |  |
| alternative dictionary used: MedDRA 15.1        |                   |                    |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0              |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0              |  |
| nodal rhythm                                    |                   |                    |  |
| alternative dictionary used: MedDRA 15.1        |                   |                    |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| palpitations                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pericardial effusion                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pericardial haemorrhage                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| pericarditis                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| postinfarction angina                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| prinzmetal angina                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                   |                  |  |  |
|---|-------------------|------------------|--|--|
| right ventricular failure<br>alternative dictionary used:<br>MedDRA 15.1    |                   |                  |  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%)  | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 3             | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 1             | 0 / 1            |  |  |
| sinus arrest<br>alternative dictionary used:<br>MedDRA 15.1                 |                   |                  |  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 2             | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0             | 0 / 0            |  |  |
| sinus bradycardia<br>alternative dictionary used:<br>MedDRA 15.1            |                   |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 0             | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0             | 0 / 0            |  |  |
| sinus node dysfunction<br>alternative dictionary used:<br>MedDRA 15.1       |                   |                  |  |  |
| subjects affected / exposed   | 12 / 6036 (0.20%) | 9 / 6052 (0.15%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 12            | 0 / 9            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0             | 0 / 0            |  |  |
| sinus tachycardia<br>alternative dictionary used:<br>MedDRA 15.1            |                   |                  |  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 2             | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0             | 0 / 0            |  |  |
| stress cardiomyopathy<br>alternative dictionary used:<br>MedDRA 15.1        |                   |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                          | 0 / 0             | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                               | 0 / 0             | 0 / 0            |  |  |
| supraventricular tachycardia<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| systolic dysfunction                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tachyarrhythmia                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tachycardia                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ventricle rupture                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ventricular arrhythmia                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 2            |  |
| ventricular extrasystoles                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| ventricular fibrillation<br>alternative dictionary used:<br>MedDRA 15.1                |                   |                   |  |
| subjects affected / exposed  | 7 / 6036 (0.12%)  | 10 / 6052 (0.17%) |  |
| occurrences causally related to<br>treatment / all                                     | 0 / 7             | 0 / 10            |  |
| deaths causally related to<br>treatment / all  | 0 / 2             | 0 / 3             |  |
| ventricular hypokinesia<br>alternative dictionary used:<br>MedDRA 15.1                 |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all                                     | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |
| ventricular tachyarrhythmia<br>alternative dictionary used:<br>MedDRA 15.1             |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all                                     | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |
| ventricular tachycardia<br>alternative dictionary used:<br>MedDRA 15.1                 |                   |                   |  |
| subjects affected / exposed  | 16 / 6036 (0.27%) | 24 / 6052 (0.40%) |  |
| occurrences causally related to<br>treatment / all                                     | 0 / 21            | 0 / 24            |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |
| wolff-parkinson-white syndrome<br>alternative dictionary used:<br>MedDRA 15.1          |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all                                     | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |
| Nervous system disorders   |                   |                   |  |
| acute disseminated<br>encephalomyelitis<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all                                     | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all  | 0 / 0             | 0 / 0             |  |
| amyotrophic lateral sclerosis<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| aphasia   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ataxia  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| autonomic nervous system imbalance              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| brain injury                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| brain mass                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| brain stem stroke                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| carotid arteriosclerosis                        |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| carotid artery disease                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 4 / 6052 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| carotid artery occlusion                        |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| carotid artery stenosis                         |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 21 / 6036 (0.35%) | 39 / 6052 (0.64%) |  |
| occurrences causally related to treatment / all | 0 / 21            | 0 / 42            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| carotid sinus syndrome                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| carpal tunnel syndrome                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| cerebellar ischaemia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed      | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cerebral arteriosclerosis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cerebellar syndrome<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed       | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cerebral artery occlusion<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cerebral haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed      | 3 / 6036 (0.05%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all  | 0 / 3            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 1            | 0 / 2            |  |  |
| cerebral infarction<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed       | 5 / 6036 (0.08%) | 4 / 6052 (0.07%) |  |  |
| occurrences causally related to<br>treatment / all  | 2 / 5            | 1 / 4            |  |  |
| deaths causally related to<br>treatment / all   | 0 / 0            | 0 / 0            |  |  |
| cerebral ischaemia<br>alternative dictionary used:<br>MedDRA 15.1                                       |                  |                  |  |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all                              | 0 / 1             | 0 / 4             |  |
| deaths causally related to treatment / all                                   | 0 / 0             | 0 / 0             |  |
| cerebrovascular insufficiency<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                              | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                                   | 0 / 0             | 0 / 1             |  |
| cerebrovascular accident<br>alternative dictionary used:<br>MedDRA 15.1      |                   |                   |  |
| subjects affected / exposed  | 61 / 6036 (1.01%) | 62 / 6052 (1.02%) |  |
| occurrences causally related to treatment / all                              | 0 / 63            | 0 / 65            |  |
| deaths causally related to treatment / all                                   | 0 / 7             | 0 / 10            |  |
| cervical myelopathy<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                              | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                                   | 0 / 0             | 0 / 0             |  |
| cervical radiculopathy<br>alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all                              | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all                                   | 0 / 0             | 0 / 0             |  |
| cognitive disorder<br>alternative dictionary used:<br>MedDRA 15.1            |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                              | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all                                   | 0 / 0             | 0 / 0             |  |
| complex partial seizures<br>alternative dictionary used:<br>MedDRA 15.1      |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                              | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                                   | 0 / 0             | 0 / 1             |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| complex regional pain syndrome<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| dementia alzheimer's type<br>alternative dictionary used:<br>MedDRA 15.1      |                  |                  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 3            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 1            | 0 / 0            |  |
| dementia<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 4            | 0 / 3            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| diabetic neuropathy<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed   | 6 / 6036 (0.10%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 9            | 0 / 2            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| dizziness<br>alternative dictionary used:<br>MedDRA 15.1                      |                  |                  |  |
| subjects affected / exposed   | 6 / 6036 (0.10%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 6            | 0 / 7            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| embolic cerebral infarction<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| embolic stroke<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| encephalopathy                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 4 / 6036 (0.07%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| epilepsy  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| essential tremor                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| guillain-barre syndrome                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| haemorrhage intracranial                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| haemorrhagic stroke                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 2            | 0 / 3            |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| haemorrhagic transformation stroke<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                                | 0 / 0            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                     | 0 / 0            | 0 / 1            |  |  |
| headache<br>alternative dictionary used:<br>MedDRA 15.1                           |                  |                  |  |  |
| subjects affected / exposed   | 7 / 6036 (0.12%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                                | 1 / 7            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                     | 0 / 0            | 0 / 0            |  |  |
| hemiparesis<br>alternative dictionary used:<br>MedDRA 15.1                        |                  |                  |  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                                | 0 / 3            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                                     | 0 / 0            | 0 / 0            |  |  |
| hypoesthesia<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                                | 0 / 0            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                     | 0 / 0            | 0 / 0            |  |  |
| hypoglycaemic coma<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                                     | 0 / 0            | 0 / 0            |  |  |
| hypoxic-ischaemic encephalopathy<br>alternative dictionary used:<br>MedDRA 15.1   |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                                | 0 / 1            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                     | 0 / 0            | 0 / 1            |  |  |
| intraventricular haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| ischaemic stroke                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 25 / 6036 (0.41%) | 18 / 6052 (0.30%) |  |
| occurrences causally related to treatment / all | 1 / 25            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 3             |  |
| lacunar infarction                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| loss of consciousness                           |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| lumbar radiculopathy                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| lumbosacral radiculopathy                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| metabolic encephalopathy                        |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%)  | 5 / 6052 (0.08%)  |  |
| occurrences causally related to treatment / all | 0 / 3             | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 1             | 0 / 0             |  |

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| migraine   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 5 / 6036 (0.08%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 5            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| moyamoya disease                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| myasthenia gravis                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 2 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| myelitis transverse                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| myoclonus  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| nerve root compression                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| nerve compression                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| nervous system disorder                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| neuralgia                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| neuropathy peripheral                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| normal pressure hydrocephalus                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| paraesthesia                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| parkinson's disease                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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|--|------------------|------------------|--|
| partial seizures                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| peroneal nerve palsy                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| polyneuropathy                                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| post herpetic neuralgia                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| postictal paralysis                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| presyncope   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 8 / 6036 (0.13%) | 9 / 6052 (0.15%) |  |
| occurrences causally related to<br>treatment / all | 0 / 9            | 0 / 9            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| quadriparesis                                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| quadriplegia                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| radicular syndrome                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| radiculopathy                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| restless legs syndrome                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| sciatica  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| seizure   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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| spinal claudication                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| spinal cord compression                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| spinal cord infarction                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| spinal cord oedema                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| status epilepticus                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| subarachnoid haemorrhage                           |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 1            |  |
| syncope  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 46 / 6036 (0.76%) | 52 / 6052 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 48            | 1 / 54            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| thalamus haemorrhage                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| thrombotic stroke                               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| toxic encephalopathy                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| transient global amnesia                        |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| transient ischaemic attack                      |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 37 / 6036 (0.61%) | 39 / 6052 (0.64%) |  |
| occurrences causally related to treatment / all | 1 / 44            | 0 / 42            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| tremor  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| trigeminal neuralgia                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| uraemic encephalopathy                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| vascular encephalopathy                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| vascular dementia                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| vasogenic cerebral oedema                          |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| vertebral artery stenosis                          |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| vertebrobasilar insufficiency                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| vertigo cns origin                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| viith nerve paralysis                           |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| vith nerve paresis                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| vith nerve paralysis                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Blood and lymphatic system disorders            |                   |                   |  |
| anaemia   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 30 / 6036 (0.50%) | 38 / 6052 (0.63%) |  |
| occurrences causally related to treatment / all | 0 / 31            | 2 / 46            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| aplastic anaemia                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| coagulopathy                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cytopenia                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| disseminated intravascular coagulation          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| febrile neutropenia                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| haemorrhagic anaemia                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| heparin-induced thrombocytopenia                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| immune thrombocytopenic purpura<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| iron deficiency anaemia<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all                                | 0 / 2            | 0 / 5            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| leukocytosis<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 4            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| lymphadenitis<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| lymphadenopathy<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |
| lymphadenopathy mediastinal<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| microcytic anaemia                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| normochromic normocytic anaemia                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 1 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| pancytopenia                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| pernicious anaemia                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| splenic infarction                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| spontaneous haemorrhage                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| thrombocytopenia                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Ear and labyrinth disorders                     |                  |                  |  |
| conductive deafness                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| deafness neurosensory                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ear pain  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| eustachian tube dysfunction                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| meniere's disease                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| otosclerosis                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| tinnitus  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| vertigo   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%)  | 15 / 6052 (0.25%) |  |
| occurrences causally related to treatment / all | 0 / 7             | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| vertigo positional                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Eye disorders                                   |                   |                   |  |
| age-related macular degeneration                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cataract  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 15 / 6036 (0.25%) | 14 / 6052 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 19            | 2 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cataract nuclear                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                         | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| conjunctival haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                         | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| diabetic retinopathy<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| diplopia<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| ectropion<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                         | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| entropion<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |
| eye haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                         | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                              | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| eye pain   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| eyelid ptosis                                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| glaucoma   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| idiopathic orbital inflammation                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| iridocyclitis                                      |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| iritis   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| keratitis  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| keratopathy                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| lens dislocation                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| macular fibrosis                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| open angle glaucoma                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| optic atrophy                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (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                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| optic neuropathy                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| retinal artery occlusion                           |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| retinal detachment                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 1 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| retinal haemorrhage                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| retinopathy  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| visual acuity reduced                              |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| visual impairment                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vitreous haemorrhage                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrointestinal disorders                      |                  |                  |  |
| abdominal adhesions                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| abdominal compartment syndrome                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| abdominal distension                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| abdominal hernia                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| abdominal mass                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| abdominal pain                                  |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 18 / 6036 (0.30%) | 8 / 6052 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 20            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| abdominal pain upper                            |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%)  | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 5             | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| abdominal strangulated hernia                   |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| abdominal wall cyst                             |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| abdominal wall haematoma                        |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| alcoholic pancreatitis                          |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| anal haemorrhage                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| ascites  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| chronic gastritis                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| coeliac artery stenosis                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| colitis  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 5 / 6036 (0.08%) | 9 / 6052 (0.15%) |  |
| occurrences causally related to<br>treatment / all | 0 / 5            | 0 / 9            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 1            |  |
| colitis ischaemic                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 2 / 7            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| colitis microscopic                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| colitis ulcerative                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| colonic fistula                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| constipation                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%) | 8 / 6052 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| crohn's disease                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| diarrhoea                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| dieulafoy's vascular malformation               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |  |
|---|------------------|------------------|--|--|
| diverticular perforation<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                  | 0 / 1            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                                       | 0 / 0            | 0 / 0            |  |  |
| diverticulum<br>alternative dictionary used:<br>MedDRA 15.1                         |                  |                  |  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                  | 0 / 1            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                                       | 0 / 0            | 0 / 0            |  |  |
| diverticulum intestinal<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                                  | 0 / 2            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                                       | 0 / 0            | 0 / 0            |  |  |
| diverticulum intestinal haemorrhagic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed   | 5 / 6036 (0.08%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                                  | 0 / 5            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                       | 0 / 0            | 0 / 0            |  |  |
| duodenal ulcer<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |  |
| subjects affected / exposed   | 3 / 6036 (0.05%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all                                  | 0 / 3            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all                                       | 0 / 0            | 0 / 0            |  |  |
| duodenal stenosis<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                                  | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                                       | 0 / 0            | 0 / 0            |  |  |
| duodenal ulcer haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                           | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all                                | 0 / 0            | 0 / 0            |  |
| duodenal ulcer perforation<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all                           | 0 / 0            | 0 / 3            |  |
| deaths causally related to treatment / all                                | 0 / 0            | 0 / 0            |  |
| duodenitis<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                           | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                | 0 / 0            | 0 / 0            |  |
| dyspepsia<br>alternative dictionary used:<br>MedDRA 15.1                  |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                           | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all                                | 0 / 0            | 0 / 0            |  |
| dysphagia<br>alternative dictionary used:<br>MedDRA 15.1                  |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                           | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all                                | 0 / 0            | 0 / 0            |  |
| enteritis<br>alternative dictionary used:<br>MedDRA 15.1                  |                  |                  |  |
| subjects affected / exposed   | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                           | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all                                | 0 / 0            | 0 / 0            |  |
| enterocolitis<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                           | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                | 0 / 0            | 0 / 0            |  |

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|--|------------------------------------|------------------------------------|--|--|
| enterovesical fistula<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| erosive oesophagitis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| faecal incontinence<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| faecaloma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all             | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 4 / 6052 (0.07%)<br>0 / 4<br>0 / 0 |  |  |
| femoral hernia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| food poisoning<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| gastric cyst<br>alternative dictionary used:<br>MedDRA 15.1  |                                    |                                    |  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| gastric disorder                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| gastric haemorrhage                             |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| gastric polyps                                  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| gastric ulcer                                   |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%)  | 7 / 6052 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 6             | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| gastric ulcer haemorrhage                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| gastritis                                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 10 / 6036 (0.17%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |



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|--|------------------|------------------|--|--|
| gastric ulcer perforation<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| gastritis alcoholic<br>alternative dictionary used:<br>MedDRA 15.1                             |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| gastritis erosive<br>alternative dictionary used:<br>MedDRA 15.1                               |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| gastritis haemorrhagic<br>alternative dictionary used:<br>MedDRA 15.1                          |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 1            | 0 / 0            |  |  |
| gastrointestinal angiodysplasia<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| gastrointestinal angiodysplasia<br>haemorrhagic<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| gastrointestinal disorder<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                                   | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| gastrointestinal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1       |                   |                   |  |
| subjects affected / exposed   | 32 / 6036 (0.53%) | 26 / 6052 (0.43%) |  |
| occurrences causally related to treatment / all                                   | 1 / 32            | 0 / 32            |  |
| deaths causally related to treatment / all  | 0 / 1             | 0 / 2             |  |
| gastrointestinal inflammation<br>alternative dictionary used:<br>MedDRA 15.1      |                   |                   |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                   | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| gastrointestinal ulcer haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                   | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| gastrooesophageal reflux disease<br>alternative dictionary used:<br>MedDRA 15.1   |                   |                   |  |
| subjects affected / exposed   | 13 / 6036 (0.22%) | 11 / 6052 (0.18%) |  |
| occurrences causally related to treatment / all                                   | 1 / 13            | 0 / 11            |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| gingival bleeding<br>alternative dictionary used:<br>MedDRA 15.1                  |                   |                   |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                   | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| glossitis<br>alternative dictionary used:<br>MedDRA 15.1                          |                   |                   |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                   | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |

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| haematemesis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all              | <br><br><br>3 / 6036 (0.05%)<br>0 / 3<br>0 / 1 | <br><br><br>1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| haematochezia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all             | <br><br><br>3 / 6036 (0.05%)<br>0 / 3<br>0 / 0 | <br><br><br>1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| haemorrhoidal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | <br><br><br>2 / 6036 (0.03%)<br>0 / 2<br>0 / 0 | <br><br><br>1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| haemorrhoids<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all              | <br><br><br>4 / 6036 (0.07%)<br>0 / 4<br>0 / 0 | <br><br><br>2 / 6052 (0.03%)<br>0 / 2<br>0 / 0 |  |  |
| heyde's syndrome<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | <br><br><br>1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | <br><br><br>0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| hiatus hernia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all             | <br><br><br>4 / 6036 (0.07%)<br>0 / 4<br>0 / 0 | <br><br><br>2 / 6052 (0.03%)<br>0 / 2<br>0 / 0 |  |  |
| ileus<br>alternative dictionary used:<br>MedDRA 15.1   |  |  |  |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| subjects affected / exposed  | 5 / 6036 (0.08%)  | 5 / 6052 (0.08%)  |  |
| occurrences causally related to treatment / all                          | 0 / 5             | 0 / 5             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| impaired gastric emptying<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed  | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                          | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| inguinal hernia<br>alternative dictionary used:<br>MedDRA 15.1           |                   |                   |  |
| subjects affected / exposed  | 15 / 6036 (0.25%) | 13 / 6052 (0.21%) |  |
| occurrences causally related to treatment / all                          | 0 / 15            | 0 / 14            |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| intestinal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1    |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                          | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| intestinal ischaemia<br>alternative dictionary used:<br>MedDRA 15.1      |                   |                   |  |
| subjects affected / exposed  | 5 / 6036 (0.08%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                          | 0 / 6             | 0 / 1             |  |
| deaths causally related to treatment / all                               | 0 / 1             | 0 / 0             |  |
| intestinal infarction<br>alternative dictionary used:<br>MedDRA 15.1     |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                          | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |
| intestinal obstruction<br>alternative dictionary used:<br>MedDRA 15.1    |                   |                   |  |
| subjects affected / exposed  | 2 / 6036 (0.03%)  | 6 / 6052 (0.10%)  |  |
| occurrences causally related to treatment / all                          | 0 / 2             | 0 / 6             |  |
| deaths causally related to treatment / all                               | 0 / 0             | 0 / 0             |  |

|  |                                    |                                    |  |  |
|--|------------------------------------|------------------------------------|--|--|
| intestinal perforation<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all      | 2 / 6036 (0.03%)<br>0 / 2<br>0 / 1 | 3 / 6052 (0.05%)<br>0 / 3<br>0 / 1 |  |  |
| intestinal prolapse<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all         | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| intra-abdominal haematoma<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| intra-abdominal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| irritable bowel syndrome<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | 0 / 6036 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| jejunal perforation<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all         | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0 | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| large intestinal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1  |                                    |                                    |  |  |

|  |                  |                   |  |
|--|------------------|-------------------|--|
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all  | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0             |  |
| large intestinal obstruction<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 1             |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0             |  |
| large intestinal stenosis<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0             |  |
| large intestine perforation<br>alternative dictionary used:<br>MedDRA 15.1               |                  |                   |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all  | 0 / 2            | 0 / 2             |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0             |  |
| large intestine polyp<br>alternative dictionary used:<br>MedDRA 15.1                     |                  |                   |  |
| subjects affected / exposed  | 6 / 6036 (0.10%) | 11 / 6052 (0.18%) |  |
| occurrences causally related to treatment / all  | 0 / 7            | 1 / 12            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0             |  |
| localised intraabdominal fluid collection<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all  | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0             |  |
| lower gastrointestinal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| mallory-weiss syndrome                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| melaena   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| mesenteric vascular insufficiency               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| mouth haemorrhage                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| nausea  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 8 / 6036 (0.13%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to treatment / all | 1 / 8            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| odynophagia                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| oedematous pancreatitis                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| oesophageal achalasia                              |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| oesophageal oedema                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| oesophageal spasm                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| oesophageal stenosis                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| oesophageal ulcer                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| oesophagitis                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |



|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pancreatic mass                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pancreatic pseudocyst                           |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pancreatitis                                    |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 12 / 6036 (0.20%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all | 1 / 13            | 2 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pancreatitis acute                              |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 10 / 6036 (0.17%) | 6 / 6052 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 10            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pancreatitis chronic                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| pancreatitis haemorrhagic                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| pancreatitis necrotising                           |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| peptic ulcer haemorrhage                           |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| peptic ulcer                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| peritoneal adhesions                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| pneumoperitoneum                                   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| rectal haemorrhage                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| rectal polyp                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                             | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |
| rectal ulcer haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1     |                   |                   |  |
| subjects affected / exposed   | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                             | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 1             |  |
| retroperitoneal effusion<br>alternative dictionary used:<br>MedDRA 15.1     |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                             | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |
| retroperitoneal haematoma<br>alternative dictionary used:<br>MedDRA 15.1    |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                             | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |
| retroperitoneal haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                             | 0 / 1             | 0 / 3             |  |
| deaths causally related to treatment / all                                  | 0 / 1             | 0 / 0             |  |
| salivary gland mass<br>alternative dictionary used:<br>MedDRA 15.1          |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                             | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                                  | 0 / 0             | 0 / 0             |  |
| small intestinal obstruction<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 11 / 6036 (0.18%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all                             | 0 / 12            | 0 / 11            |  |
| deaths causally related to treatment / all                                  | 0 / 1             | 0 / 0             |  |

|  |                  |                  |  |  |
|--|------------------|------------------|--|--|
| small intestinal perforation                       |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| subileus   |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| swollen tongue                                     |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 1 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| tongue haemorrhage                                 |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| tongue oedema                                      |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| umbilical hernia                                   |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%) | 6 / 6052 (0.10%) |  |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 6            |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |  |
| upper gastrointestinal haemorrhage                 |                  |                  |  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 11 / 6036 (0.18%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all | 0 / 12            | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| volvulus  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| vomiting  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 9 / 6036 (0.15%)  | 7 / 6052 (0.12%)  |  |
| occurrences causally related to treatment / all | 1 / 12            | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Skin and subcutaneous tissue disorders          |                   |                   |  |
| angioedema                                      |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| decubitus ulcer                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| dermal cyst                                     |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| dermatomyositis                                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| diabetic foot                                   |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 10 / 6036 (0.17%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 11            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| diabetic neuropathic ulcer                      |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| erythema multiforme                             |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| henoch-schonlein purpura                        |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| hyperhidrosis                                   |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| hyperkeratosis                                  |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |

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|--|------------------|------------------|--|--|
| hypersensitivity vasculitis<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                         | 1 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| psoriasis<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| rash<br>alternative dictionary used:<br>MedDRA 15.1                        |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 1            | 1 / 2            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| skin lesion<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                         | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| skin ulcer<br>alternative dictionary used:<br>MedDRA 15.1                  |                  |                  |  |  |
| subjects affected / exposed  | 9 / 6036 (0.15%) | 5 / 6052 (0.08%) |  |  |
| occurrences causally related to<br>treatment / all                         | 1 / 9            | 0 / 6            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| urticaria<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                         | 1 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                              | 0 / 0            | 0 / 0            |  |  |
| vasculitic rash<br>alternative dictionary used:<br>MedDRA 15.1             |                  |                  |  |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| Renal and urinary disorders                     |                   |                   |  |
| acute kidney injury                             |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 48 / 6036 (0.80%) | 67 / 6052 (1.11%) |  |
| occurrences causally related to treatment / all | 0 / 58            | 2 / 81            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 3             |  |
| acute prerenal failure                          |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| azotaemia                                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| bladder outlet obstruction                      |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| bladder prolapse                                |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| calculus ureteric                               |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |



|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 9 / 6052 (0.15%)  |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 9             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| calculus urinary                                |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| chronic kidney disease                          |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 9 / 6036 (0.15%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to treatment / all | 1 / 10           | 3 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 1             |  |
| cystitis haemorrhagic                           |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| cystitis ulcerative                             |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| diabetic nephropathy                            |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| dysuria   |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| glomerulonephritis                                 |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| glomerulosclerosis                                 |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| haematuria   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 11 / 6036 (0.18%) | 4 / 6052 (0.07%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 14            | 0 / 4             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hydronephrosis                                     |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 5 / 6052 (0.08%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 5             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypotonic urinary bladder                          |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| nephrolithiasis                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 19 / 6036 (0.31%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 20            | 0 / 12            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| nephropathy  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| nephrosclerosis                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| nephrotic syndrome                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| obstructive uropathy                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pelvi-ureteric obstruction                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| prerenal failure                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| renal artery stenosis                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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| renal colic  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| renal cyst   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| renal failure                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 14 / 6036 (0.23%) | 11 / 6052 (0.18%) |  |
| occurrences causally related to<br>treatment / all | 0 / 16            | 0 / 11            |  |
| deaths causally related to<br>treatment / all      | 0 / 1             | 0 / 2             |  |
| renal haematoma                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| renal impairment                                   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 3 / 6036 (0.05%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 3             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 1             |  |
| renal infarct                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| renal injury                                       |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                             | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| renal tubular necrosis<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                             | 0 / 1            | 1 / 2            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| renal vein thrombosis<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                             | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| stress urinary incontinence<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                             | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| tubulointerstitial nephritis<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                             | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| ureteral disorder<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                             | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |
| urethral haemorrhage<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                             | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                  | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| urethral stenosis                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 3            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| urinary bladder haemorrhage                        |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| urinary incontinence                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| urinary retention                                  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 9 / 6052 (0.15%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 9            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| urinary tract obstruction                          |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| Endocrine disorders                                |                  |                  |  |
| autoimmune thyroiditis                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| goitre   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| hyperparathyroidism                             |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| hyperparathyroidism primary                     |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| Musculoskeletal and connective tissue disorders |                  |                   |  |
| ankylosing spondylitis                          |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| arthralgia                                      |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 17 / 6052 (0.28%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| arthritis                                       |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 9 / 6036 (0.15%) | 7 / 6052 (0.12%)  |  |
| occurrences causally related to treatment / all | 0 / 10           | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| arthropathy                                     |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed                     | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| back pain                                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 15 / 6036 (0.25%) | 14 / 6052 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| bone pain                                       |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| bursitis  |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| cervical spinal stenosis                        |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| chondrocalcinosis pyrophosphate                 |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |
| compartment syndrome                            |                   |                   |  |
| alternative dictionary used: MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0             |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| costochondritis                                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| dupuytren's contracture                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| facet joint syndrome                               |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| fibromyalgia                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| foot deformity                                     |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 0 / 4            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| gouty arthritis                                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| groin pain   |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                   |  |
|---|------------------|-------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| haemarthrosis                                   |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| intervertebral disc degeneration                |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 6 / 6052 (0.10%)  |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| intervertebral disc disorder                    |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| intervertebral disc protrusion                  |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 14 / 6052 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| joint instability                               |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |
| joint swelling                                  |                  |                   |  |
| alternative dictionary used: MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0             |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| kyphosis   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| ligament laxity                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| lumbar spinal stenosis                             |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 13 / 6036 (0.22%) | 23 / 6052 (0.38%) |  |
| occurrences causally related to<br>treatment / all | 0 / 13            | 1 / 24            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| mobility decreased                                 |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| muscle haemorrhage                                 |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 4 / 6052 (0.07%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 4             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| muscle spasms                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| muscular weakness                                  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed   | 4 / 6036 (0.07%)  | 4 / 6052 (0.07%)  |  |
| occurrences causally related to treatment / all                           | 0 / 4             | 0 / 4             |  |
| deaths causally related to treatment / all                                | 0 / 0             | 0 / 0             |  |
| musculoskeletal chest pain<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 17 / 6036 (0.28%) | 15 / 6052 (0.25%) |  |
| occurrences causally related to treatment / all                           | 0 / 18            | 0 / 15            |  |
| deaths causally related to treatment / all                                | 0 / 0             | 0 / 0             |  |
| musculoskeletal discomfort<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                           | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                                | 0 / 0             | 0 / 0             |  |
| musculoskeletal pain<br>alternative dictionary used:<br>MedDRA 15.1       |                   |                   |  |
| subjects affected / exposed   | 5 / 6036 (0.08%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                           | 0 / 6             | 0 / 0             |  |
| deaths causally related to treatment / all                                | 0 / 0             | 0 / 0             |  |
| musculoskeletal stiffness<br>alternative dictionary used:<br>MedDRA 15.1  |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                           | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                                | 0 / 0             | 0 / 0             |  |
| myalgia<br>alternative dictionary used:<br>MedDRA 15.1                    |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                           | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all                                | 0 / 0             | 0 / 0             |  |
| neck pain<br>alternative dictionary used:<br>MedDRA 15.1                  |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 4 / 6052 (0.07%)  |  |
| occurrences causally related to treatment / all                           | 0 / 2             | 0 / 4             |  |
| deaths causally related to treatment / all                                | 0 / 0             | 0 / 0             |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| neuropathic arthropathy                            |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| osteitis   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 1             |  |
| osteoarthritis                                     |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 70 / 6036 (1.16%) | 66 / 6052 (1.09%) |  |
| occurrences causally related to<br>treatment / all | 0 / 76            | 1 / 75            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| osteochondrosis                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| osteonecrosis                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| pain in extremity                                  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 7 / 6036 (0.12%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 2 / 7             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| pain in jaw  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| polymyalgia rheumatica                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pseudarthrosis                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| rhabdomyolysis                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 1 / 6            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| rheumatoid arthritis                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| rotator cuff syndrome                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 8 / 6036 (0.13%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 8            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| scoliosis                                       |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                   |  |
|--|------------------|-------------------|--|
| spinal column stenosis                             |                  |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                        | 6 / 6036 (0.10%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 6            | 0 / 10            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 1             |  |
| spinal osteoarthritis                              |                  |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                        | 5 / 6036 (0.08%) | 8 / 6052 (0.13%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 5            | 0 / 9             |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0             |  |
| spinal pain  |                  |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                        | 5 / 6036 (0.08%) | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 5            | 0 / 3             |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0             |  |
| spondylolisthesis                                  |                  |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%) | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 4            | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0             |  |
| synovial cyst                                      |                  |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0             |  |
| synovitis  |                  |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0             |  |
| tendon disorder                                    |                  |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| tendonitis                                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| trigger finger                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| vertebral foraminal stenosis                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| abdominal abscess                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| abdominal infection                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| abdominal sepsis                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 1            |  |
| abdominal wall abscess<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| abdominal wall infection<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| abscess<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| abscess limb<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |
| subjects affected / exposed  | 3 / 6036 (0.05%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all                          | 0 / 3            | 0 / 4            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| abscess neck<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| abscess of salivary gland<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| abscess oral                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| acute sinusitis                                    |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| anal abscess                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| appendicitis                                       |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 9 / 6036 (0.15%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to<br>treatment / all | 0 / 9            | 0 / 5            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| appendicitis perforated                            |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arteriosclerotic gangrene                          |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| arteritis infective                                |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| arthritis bacterial                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| atypical pneumonia                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bacterial infection                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bacteraemia                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| bacterial sepsis                                |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| biliary sepsis                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| biliary tract infection                            |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| breast cellulitis                                  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| bronchitis   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 25 / 6036 (0.41%) | 18 / 6052 (0.30%) |  |
| occurrences causally related to<br>treatment / all | 0 / 25            | 0 / 18            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| bronchitis viral                                   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| bursitis infective                                 |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 3             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| cellulitis   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 41 / 6036 (0.68%) | 42 / 6052 (0.69%) |  |
| occurrences causally related to<br>treatment / all | 0 / 48            | 0 / 45            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| cellulitis staphylococcal                          |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cholangitis infective                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| cholecystitis infective                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 5 / 6036 (0.08%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 5            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| chronic sinusitis                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| clostridium difficile colitis                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 8 / 6052 (0.13%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 10           |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| clostridium difficile infection                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| clostridium difficile sepsis                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|   |                                      |                                    |  |  |
|---|--------------------------------------|------------------------------------|--|--|
| colonic abscess<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| cystitis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                 | 6 / 6036 (0.10%)<br>0 / 6<br>0 / 0   | 2 / 6052 (0.03%)<br>0 / 2<br>0 / 0 |  |  |
| device related infection<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0   | 2 / 6052 (0.03%)<br>0 / 2<br>0 / 0 |  |  |
| diabetic foot infection<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0 |  |  |
| diabetic gangrene<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 2 / 6036 (0.03%)<br>0 / 2<br>0 / 0   | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| diverticulitis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all           | 13 / 6036 (0.22%)<br>0 / 13<br>0 / 0 | 5 / 6052 (0.08%)<br>0 / 5<br>0 / 0 |  |  |
| endocarditis<br>alternative dictionary used:<br>MedDRA 15.1   |                                      |                                    |  |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 4            | 0 / 2            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| endocarditis bacterial<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| endocarditis enterococcal<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| endophthalmitis<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| enterobacter infection<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| enterococcal bacteraemia<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                          | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |
| enterococcal infection<br>alternative dictionary used:<br>MedDRA 15.1    |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                          | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all                               | 0 / 0            | 0 / 0            |  |

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|--|------------------|------------------|--|--|
| enterococcal sepsis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed          | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| epididymitis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed <sup>[39]</sup> | 1 / 4648 (0.02%) | 1 / 4658 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| erysipelas<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed                   | 6 / 6036 (0.10%) | 5 / 6052 (0.08%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 8            | 0 / 5            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| escherichia bacteraemia<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed      | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 2            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| escherichia infection<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| escherichia pyelonephritis<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all   | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all  | 0 / 0            | 0 / 0            |  |  |
| escherichia sepsis<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |  |



|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| escherichia urinary tract infection<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| extradural abscess<br>alternative dictionary used:<br>MedDRA 15.1                  |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| febrile infection<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| folliculitis<br>alternative dictionary used:<br>MedDRA 15.1                        |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| gallbladder abscess<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                                    | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |
| gallbladder empyema<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                                    | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all   | 0 / 0            | 0 / 0            |  |

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|--|-------------------|-------------------|--|
| gangrene   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 7 / 6036 (0.12%)  | 11 / 6052 (0.18%) |  |
| occurrences causally related to<br>treatment / all | 0 / 7             | 0 / 14            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| gastritis viral                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 1             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| gastroenteritis                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 16 / 6036 (0.27%) | 16 / 6052 (0.26%) |  |
| occurrences causally related to<br>treatment / all | 0 / 19            | 0 / 16            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| gastroenteritis norovirus                          |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| gastroenteritis viral                              |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 8 / 6036 (0.13%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 8             | 0 / 3             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| giardiasis   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| graft infection                                    |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| groin abscess                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| h1n1 influenza                                  |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| haematoma infection                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hepatitis c                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hepatitis viral                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| herpes zoster                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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|--|------------------|------------------|--|--|
| implant site cellulitis<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0            | 0 / 0            |  |  |
| implant site infection<br>alternative dictionary used:<br>MedDRA 15.1  |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0            | 0 / 0            |  |  |
| incision site infection<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 2            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0            | 0 / 0            |  |  |
| infected bite<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0            | 0 / 0            |  |  |
| infected fistula<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 0            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0            | 0 / 0            |  |  |
| infected seroma<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                     | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                          | 0 / 0            | 0 / 0            |  |  |
| infected skin ulcer<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                                   | 4 / 6036 (0.07%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all               | 0 / 4             | 0 / 1            |  |
| deaths causally related to treatment / all                    | 0 / 0             | 0 / 0            |  |
| infection   |                   |                  |  |
| alternative dictionary used: MedDRA 15.1                      |                   |                  |  |
| subjects affected / exposed                                   | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all               | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all                    | 0 / 0             | 0 / 0            |  |
| infectious colitis  |                   |                  |  |
| alternative dictionary used: MedDRA 15.1                      |                   |                  |  |
| subjects affected / exposed                                   | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all               | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all                    | 0 / 0             | 0 / 0            |  |
| infectious pleural effusion                                   |                   |                  |  |
| alternative dictionary used: MedDRA 15.1                      |                   |                  |  |
| subjects affected / exposed                                   | 0 / 6036 (0.00%)  | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all               | 0 / 0             | 0 / 2            |  |
| deaths causally related to treatment / all                    | 0 / 0             | 0 / 1            |  |
| infective exacerbation of chronic obstructive airways disease |                   |                  |  |
| alternative dictionary used: MedDRA 15.1                      |                   |                  |  |
| subjects affected / exposed                                   | 1 / 6036 (0.02%)  | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all               | 0 / 1             | 0 / 4            |  |
| deaths causally related to treatment / all                    | 0 / 0             | 0 / 0            |  |
| influenza   |                   |                  |  |
| alternative dictionary used: MedDRA 15.1                      |                   |                  |  |
| subjects affected / exposed                                   | 11 / 6036 (0.18%) | 9 / 6052 (0.15%) |  |
| occurrences causally related to treatment / all               | 0 / 11            | 0 / 9            |  |
| deaths causally related to treatment / all                    | 0 / 0             | 0 / 0            |  |
| infusion site cellulitis                                      |                   |                  |  |
| alternative dictionary used: MedDRA 15.1                      |                   |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| infusion site infection                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| intervertebral discitis                         |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| keratitis bacterial                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| klebsiella sepsis                               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| liver abscess                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| localised infection                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| lower respiratory tract infection<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 3            | 0 / 7            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 1            |  |
| lung abscess<br>alternative dictionary used:<br>MedDRA 15.1                      |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| lung infection<br>alternative dictionary used:<br>MedDRA 15.1                    |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| mastoiditis<br>alternative dictionary used:<br>MedDRA 15.1                       |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                               | 1 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| mediastinitis<br>alternative dictionary used:<br>MedDRA 15.1                     |                  |                  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| myelitis<br>alternative dictionary used:<br>MedDRA 15.1                          |                  |                  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                               | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |
| nail bed infection<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |

|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| necrotising fasciitis                           |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| oesophageal candidiasis                         |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| orbital infection                               |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| osteomyelitis                                   |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 13 / 6036 (0.22%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to treatment / all | 0 / 15            | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| osteomyelitis acute                             |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |
| osteomyelitis bacterial                         |                   |                  |  |
| alternative dictionary used: MedDRA 15.1        |                   |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1             | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0             | 0 / 0            |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| osteomyelitis chronic<br>alternative dictionary used:<br>MedDRA 15.1          |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| parainfluenzae virus infection<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 1            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| parotitis<br>alternative dictionary used:<br>MedDRA 15.1                      |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| parvovirus infection<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| pelvic abscess<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| penile abscess<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |
| subjects affected / exposed <sup>[40]</sup>                                   | 1 / 4648 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to<br>treatment / all                            | 0 / 1            | 0 / 0            |  |
| deaths causally related to<br>treatment / all                                 | 0 / 0            | 0 / 0            |  |
| perihepatic abscess<br>alternative dictionary used:<br>MedDRA 15.1            |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| periodontitis                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| perirectal abscess                              |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| peritonitis                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 3 / 6036 (0.05%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 3            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| peritonitis bacterial                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| peritonsillar abscess                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pharyngitis                                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                    |                    |  |
|--|--------------------|--------------------|--|
| pilonidal cyst                                     |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 1 / 6036 (0.02%)   | 0 / 6052 (0.00%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 1              | 0 / 0              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| pneumonia  |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 115 / 6036 (1.91%) | 112 / 6052 (1.85%) |  |
| occurrences causally related to<br>treatment / all | 0 / 128            | 0 / 122            |  |
| deaths causally related to<br>treatment / all      | 0 / 7              | 0 / 4              |  |
| pneumonia bacterial                                |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)   | 6 / 6052 (0.10%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 2              | 0 / 6              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| pneumonia chlamydial                               |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| pneumonia fungal                                   |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)   | 1 / 6052 (0.02%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 0              | 0 / 1              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| pneumonia influenzal                               |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)   | 0 / 6052 (0.00%)   |  |
| occurrences causally related to<br>treatment / all | 0 / 3              | 0 / 0              |  |
| deaths causally related to<br>treatment / all      | 0 / 0              | 0 / 0              |  |
| pneumonia legionella                               |                    |                    |  |
| alternative dictionary used:<br>MedDRA 15.1        |                    |                    |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| pneumonia parainfluenzae viral<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| pneumonia pneumococcal<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                               | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| pneumonia staphylococcal<br>alternative dictionary used:<br>MedDRA 15.1       |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                    | 0 / 1            | 0 / 0            |  |
| pneumonia streptococcal<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed   | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                               | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| pneumonia viral<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all                               | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |
| post procedural cellulitis<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |
| subjects affected / exposed   | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all                               | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                                    | 0 / 0            | 0 / 0            |  |

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| post procedural infection<br>alternative dictionary used:<br>MedDRA 15.1     |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                           | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                                | 0 / 0            | 0 / 0            |  |  |
| post procedural sepsis<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                           | 0 / 1            | 0 / 0            |  |  |
| deaths causally related to<br>treatment / all                                | 0 / 0            | 0 / 0            |  |  |
| postoperative abscess<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                           | 0 / 0            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                | 0 / 0            | 0 / 0            |  |  |
| postoperative wound infection<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 4 / 6036 (0.07%) | 6 / 6052 (0.10%) |  |  |
| occurrences causally related to<br>treatment / all                           | 0 / 4            | 0 / 6            |  |  |
| deaths causally related to<br>treatment / all                                | 0 / 0            | 0 / 0            |  |  |
| pulmonary sepsis<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |  |
| subjects affected / exposed  | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                           | 0 / 0            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                | 0 / 0            | 0 / 1            |  |  |
| pulmonary tuberculosis<br>alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                           | 0 / 1            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                | 0 / 0            | 0 / 0            |  |  |
| pyelonephritis<br>alternative dictionary used:<br>MedDRA 15.1                |                  |                  |  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 7 / 6036 (0.12%) | 4 / 6052 (0.07%) |  |
| occurrences causally related to treatment / all | 1 / 7            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pyelonephritis acute                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| pyelonephritis chronic                          |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| respiratory syncytial virus infection           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| respiratory tract infection                     |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| respiratory tract infection viral               |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| rhinovirus infection                            |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| salmonellosis                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| sepsis   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 44 / 6036 (0.73%) | 28 / 6052 (0.46%) |  |
| occurrences causally related to<br>treatment / all | 0 / 49            | 0 / 32            |  |
| deaths causally related to<br>treatment / all      | 0 / 7             | 0 / 7             |  |
| septic shock                                       |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 10 / 6036 (0.17%) | 7 / 6052 (0.12%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 10            | 0 / 7             |  |
| deaths causally related to<br>treatment / all      | 0 / 4             | 0 / 3             |  |
| sialoadenitis                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| sinusitis  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 2             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| sinusitis fungal                                   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 0             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| skin candida                                       |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| soft tissue infection                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| spinal cord abscess                             |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 1            |  |
| staphylococcal bacteraemia                      |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 3 / 6052 (0.05%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| staphylococcal infection                        |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 6            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| staphylococcal mediastinitis                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| staphylococcal sepsis                           |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |



|  |                  |                  |  |  |
|--|------------------|------------------|--|--|
| streptococcal sepsis<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                               | 0 / 2            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |  |
| streptococcal bacteraemia<br>alternative dictionary used:<br>MedDRA 15.1         |                  |                  |  |  |
| subjects affected / exposed  | 2 / 6036 (0.03%) | 3 / 6052 (0.05%) |  |  |
| occurrences causally related to<br>treatment / all                               | 0 / 2            | 0 / 3            |  |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |  |
| subcutaneous abscess<br>alternative dictionary used:<br>MedDRA 15.1              |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                               | 0 / 1            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |  |
| tooth infection<br>alternative dictionary used:<br>MedDRA 15.1                   |                  |                  |  |  |
| subjects affected / exposed  | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                               | 0 / 1            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |  |
| tracheobronchitis<br>alternative dictionary used:<br>MedDRA 15.1                 |                  |                  |  |  |
| subjects affected / exposed  | 3 / 6036 (0.05%) | 1 / 6052 (0.02%) |  |  |
| occurrences causally related to<br>treatment / all                               | 0 / 3            | 0 / 1            |  |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |  |
| upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 15.1 |                  |                  |  |  |
| subjects affected / exposed  | 3 / 6036 (0.05%) | 2 / 6052 (0.03%) |  |  |
| occurrences causally related to<br>treatment / all                               | 0 / 3            | 0 / 2            |  |  |
| deaths causally related to<br>treatment / all                                    | 0 / 0            | 0 / 0            |  |  |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 15.1           |                  |                  |  |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| subjects affected / exposed  | 19 / 6036 (0.31%) | 32 / 6052 (0.53%) |  |
| occurrences causally related to treatment / all                                    | 0 / 22            | 0 / 36            |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 1             |  |
| urinary tract infection bacterial<br>alternative dictionary used:<br>MedDRA 15.1   |                   |                   |  |
| subjects affected / exposed  | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                    | 0 / 2             | 0 / 1             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| urinary tract infection pseudomonal<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                    | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| urosepsis<br>alternative dictionary used:<br>MedDRA 15.1                           |                   |                   |  |
| subjects affected / exposed  | 16 / 6036 (0.27%) | 14 / 6052 (0.23%) |  |
| occurrences causally related to treatment / all                                    | 0 / 17            | 0 / 14            |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 1             |  |
| vestibular neuronitis<br>alternative dictionary used:<br>MedDRA 15.1               |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                    | 0 / 0             | 0 / 1             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| viral infection<br>alternative dictionary used:<br>MedDRA 15.1                     |                   |                   |  |
| subjects affected / exposed  | 0 / 6036 (0.00%)  | 3 / 6052 (0.05%)  |  |
| occurrences causally related to treatment / all                                    | 0 / 0             | 0 / 3             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |
| viral labyrinthitis<br>alternative dictionary used:<br>MedDRA 15.1                 |                   |                   |  |
| subjects affected / exposed  | 1 / 6036 (0.02%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                                    | 0 / 1             | 0 / 0             |  |
| deaths causally related to treatment / all   | 0 / 0             | 0 / 0             |  |

|   |                                      |                                      |  |
|---|--------------------------------------|--------------------------------------|--|
| wound abscess<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0   | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0   |  |
| wound infection<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 4 / 6036 (0.07%)<br>0 / 4<br>0 / 0   | 7 / 6052 (0.12%)<br>0 / 8<br>0 / 0   |  |
| wound infection bacterial<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0   | 0 / 6052 (0.00%)<br>0 / 0<br>0 / 0   |  |
| wound infection staphylococcal<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                           | 2 / 6036 (0.03%)<br>0 / 2<br>0 / 0   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0   |  |
| Metabolism and nutrition disorders<br>decreased appetite<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 6036 (0.02%)<br>0 / 1<br>0 / 0   | 1 / 6052 (0.02%)<br>0 / 1<br>0 / 0   |  |
| dehydration<br>alternative dictionary used:<br>MedDRA 15.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 15 / 6036 (0.25%)<br>1 / 15<br>0 / 1 | 26 / 6052 (0.43%)<br>0 / 28<br>0 / 0 |  |
| diabetes mellitus<br>alternative dictionary used:<br>MedDRA 15.1  |                                      |                                      |  |

|   |                   |                   |  |
|---|-------------------|-------------------|--|
| subjects affected / exposed   | 11 / 6036 (0.18%) | 20 / 6052 (0.33%) |  |
| occurrences causally related to treatment / all                                     | 0 / 11            | 1 / 22            |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| diabetes mellitus inadequate control<br>alternative dictionary used:<br>MedDRA 15.1 |                   |                   |  |
| subjects affected / exposed   | 8 / 6036 (0.13%)  | 14 / 6052 (0.23%) |  |
| occurrences causally related to treatment / all                                     | 0 / 9             | 1 / 15            |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| diabetic ketoacidosis<br>alternative dictionary used:<br>MedDRA 15.1                |                   |                   |  |
| subjects affected / exposed   | 3 / 6036 (0.05%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to treatment / all                                     | 0 / 3             | 0 / 1             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| diabetic metabolic decompensation<br>alternative dictionary used:<br>MedDRA 15.1    |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to treatment / all                                     | 1 / 3             | 0 / 0             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| electrolyte imbalance<br>alternative dictionary used:<br>MedDRA 15.1                |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                                     | 0 / 1             | 0 / 4             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |
| failure to thrive<br>alternative dictionary used:<br>MedDRA 15.1                    |                   |                   |  |
| subjects affected / exposed   | 1 / 6036 (0.02%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                                     | 0 / 1             | 0 / 2             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 2             |  |
| fluid overload<br>alternative dictionary used:<br>MedDRA 15.1                       |                   |                   |  |
| subjects affected / exposed   | 2 / 6036 (0.03%)  | 2 / 6052 (0.03%)  |  |
| occurrences causally related to treatment / all                                     | 0 / 2             | 0 / 2             |  |
| deaths causally related to treatment / all  | 0 / 0             | 0 / 0             |  |

|  |                   |                   |  |
|--|-------------------|-------------------|--|
| gout   |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 4 / 6036 (0.07%)  | 6 / 6052 (0.10%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 4             | 0 / 6             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypercalcaemia                                     |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 1 / 6052 (0.02%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 1             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hyperglycaemia                                     |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 13 / 6036 (0.22%) | 10 / 6052 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 13            | 1 / 11            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hyperkalaemia                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 9 / 6036 (0.15%)  | 9 / 6052 (0.15%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 9             | 0 / 10            |  |
| deaths causally related to<br>treatment / all      | 0 / 1             | 0 / 0             |  |
| hyperosmolar hyperglycaemic state                  |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%)  | 0 / 6052 (0.00%)  |  |
| occurrences causally related to<br>treatment / all | 0 / 2             | 0 / 0             |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypoglycaemia                                      |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |
| subjects affected / exposed                        | 17 / 6036 (0.28%) | 18 / 6052 (0.30%) |  |
| occurrences causally related to<br>treatment / all | 1 / 17            | 0 / 18            |  |
| deaths causally related to<br>treatment / all      | 0 / 0             | 0 / 0             |  |
| hypokalaemia                                       |                   |                   |  |
| alternative dictionary used:<br>MedDRA 15.1        |                   |                   |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 6036 (0.07%) | 7 / 6052 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 4            | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hypomagnesaemia                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 2 / 6036 (0.03%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hyponatraemia                                   |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 6 / 6036 (0.10%) | 9 / 6052 (0.15%) |  |
| occurrences causally related to treatment / all | 0 / 7            | 0 / 9            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| hypovolaemia                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 2 / 6052 (0.03%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| ketoacidosis                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| lactic acidosis                                 |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| malnutrition                                    |                  |                  |  |
| alternative dictionary used: MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                     | 1 / 6036 (0.02%) | 0 / 6052 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| metabolic acidosis                                 |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 2 / 6036 (0.03%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 1            | 0 / 0            |  |
| obesity  |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 5 / 6036 (0.08%) | 5 / 6052 (0.08%) |  |
| occurrences causally related to<br>treatment / all | 0 / 5            | 0 / 5            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| type 2 diabetes mellitus                           |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 6 / 6036 (0.10%) | 6 / 6052 (0.10%) |  |
| occurrences causally related to<br>treatment / all | 4 / 6            | 2 / 6            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |
| vitamin b12 deficiency                             |                  |                  |  |
| alternative dictionary used:<br>MedDRA 15.1        |                  |                  |  |
| subjects affected / exposed                        | 0 / 6036 (0.00%) | 1 / 6052 (0.02%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0            |  |

#### Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.





[40] - The number of subjects exposed to this adverse event is less than the total number of subjects

exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

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

| <b>Non-serious adverse events</b>                     | Evacetrapib             | Placebo                 |  |
|---|-------------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events |                         |                         |  |
| subjects affected / exposed                           | 2659 / 6036<br>(44.05%) | 2529 / 6052<br>(41.79%) |  |
| Vascular disorders                                    |                         |                         |  |
| hypertension  |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1           |                         |                         |  |
| subjects affected / exposed                           | 453 / 6036 (7.50%)      | 403 / 6052 (6.66%)      |  |
| occurrences (all)                                     | 508                     | 466                     |  |
| Nervous system disorders                              |                         |                         |  |
| dizziness   |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1           |                         |                         |  |
| subjects affected / exposed                           | 389 / 6036 (6.44%)      | 352 / 6052 (5.82%)      |  |
| occurrences (all)                                     | 435                     | 407                     |  |
| Gastrointestinal disorders                            |                         |                         |  |
| diarrhoea   |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1           |                         |                         |  |
| subjects affected / exposed                           | 472 / 6036 (7.82%)      | 414 / 6052 (6.84%)      |  |
| occurrences (all)                                     | 568                     | 484                     |  |
| Respiratory, thoracic and mediastinal disorders       |                         |                         |  |
| cough   |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1           |                         |                         |  |
| subjects affected / exposed                           | 327 / 6036 (5.42%)      | 279 / 6052 (4.61%)      |  |
| occurrences (all)                                     | 367                     | 304                     |  |
| dyspnoea  |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1           |                         |                         |  |
| subjects affected / exposed                           | 305 / 6036 (5.05%)      | 307 / 6052 (5.07%)      |  |
| occurrences (all)                                     | 339                     | 341                     |  |
| Musculoskeletal and connective tissue disorders       |                         |                         |  |
| arthralgia  |                         |                         |  |
| alternative dictionary used:<br>MedDRA 15.1           |                         |                         |  |
| subjects affected / exposed                           | 375 / 6036 (6.21%)      | 370 / 6052 (6.11%)      |  |
| occurrences (all)                                     | 426                     | 425                     |  |
| back pain   |                         |                         |  |

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|--|--|--|--|
| <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>399 / 6036 (6.61%)</p> <p>442</p>   | <p>379 / 6052 (6.26%)</p> <p>412</p>   |  |
| <p>pain in extremity</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>339 / 6036 (5.62%)</p> <p>412</p>   | <p>329 / 6052 (5.44%)</p> <p>388</p>   |  |
| <p>Infections and infestations</p> <p>bronchitis</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nasopharyngitis</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>upper respiratory tract infection</p> <p>alternative dictionary used:<br/>MedDRA 15.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>363 / 6036 (6.01%)</p> <p>456</p> <p>452 / 6036 (7.49%)</p> <p>603</p> <p>327 / 6036 (5.42%)</p> <p>397</p> | <p>375 / 6052 (6.20%)</p> <p>443</p> <p>465 / 6052 (7.68%)</p> <p>602</p> <p>327 / 6052 (5.40%)</p> <p>410</p> |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported