



Clinical trial results:

A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II - IV).

The study is also known as Aliskiren Trial of Minimizing OutcomeS in Patients with HEart failure (ATMOSPHERE).

Summary

| | |
|--------------------------|---|
| EudraCT number | 2008-004104-31 |
| Trial protocol | AT DE SK NL FI SE DK LT BE PT IT IE ES CZ PL FR LV GB EE GR |
| Global end of trial date | 05 October 2015 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 20 October 2016 |
| First version publication date | 20 October 2016 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CSPP100F2301 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00853658 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |

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 | 05 October 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 October 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of ATMOSPHERE were firstly to test whether the combination of aliskiren and enalapril is superior to enalapril monotherapy in delaying time to the first occurrence of CV death or HF hospitalization in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction, and secondly to test whether aliskiren monotherapy is superior, or at least non-inferior, to enalapril monotherapy using the same composite endpoint. The superiority comparison of the combination of aliskiren and enalapril versus enalapril monotherapy in patients without diabetes at baseline was added to the primary objectives through protocol amendment #4, in April 2013.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 13 March 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 41 |
| Country: Number of subjects enrolled | Austria: 59 |
| Country: Number of subjects enrolled | Belgium: 73 |
| Country: Number of subjects enrolled | Brazil: 201 |
| Country: Number of subjects enrolled | Canada: 77 |
| Country: Number of subjects enrolled | China: 465 |
| Country: Number of subjects enrolled | Colombia: 145 |
| Country: Number of subjects enrolled | Costa Rica: 17 |
| Country: Number of subjects enrolled | Czech Republic: 307 |
| Country: Number of subjects enrolled | Denmark: 253 |
| Country: Number of subjects enrolled | Dominican Republic: 23 |
| Country: Number of subjects enrolled | Argentina: 501 |
| Country: Number of subjects enrolled | Estonia: 47 |
| Country: Number of subjects enrolled | Finland: 24 |
| Country: Number of subjects enrolled | France: 34 |
| Country: Number of subjects enrolled | Germany: 469 |

| | |
|--------------------------------------|---------------------------------------|
| Country: Number of subjects enrolled | United Kingdom: 48 |
| Country: Number of subjects enrolled | Greece: 59 |
| Country: Number of subjects enrolled | India: 782 |
| Country: Number of subjects enrolled | Ireland: 16 |
| Country: Number of subjects enrolled | Italy: 286 |
| Country: Number of subjects enrolled | Japan: 210 |
| Country: Number of subjects enrolled | Korea, Republic of: 143 |
| Country: Number of subjects enrolled | Latvia: 65 |
| Country: Number of subjects enrolled | Lithuania: 61 |
| Country: Number of subjects enrolled | Mexico: 50 |
| Country: Number of subjects enrolled | Netherlands: 162 |
| Country: Number of subjects enrolled | Norway: 22 |
| Country: Number of subjects enrolled | Peru: 116 |
| Country: Number of subjects enrolled | Poland: 302 |
| Country: Number of subjects enrolled | Portugal: 54 |
| Country: Number of subjects enrolled | Romania: 290 |
| Country: Number of subjects enrolled | Russian Federation: 554 |
| Country: Number of subjects enrolled | Slovakia: 327 |
| Country: Number of subjects enrolled | South Africa: 52 |
| Country: Number of subjects enrolled | Spain: 142 |
| Country: Number of subjects enrolled | Sweden: 141 |
| Country: Number of subjects enrolled | Switzerland: 15 |
| Country: Number of subjects enrolled | Taiwan: 113 |
| Country: Number of subjects enrolled | Thailand: 56 |
| Country: Number of subjects enrolled | Turkey: 70 |
| Country: Number of subjects enrolled | United States: 116 |
| Country: Number of subjects enrolled | Venezuela, Bolivarian Republic of: 76 |
| Worldwide total number of subjects | 7064 |
| EEA total number of subjects | 3241 |

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) | 3605 |
| From 65 to 84 years | 3357 |
| 85 years and over | 102 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During Active Run-in period, patients received enalapril for step 1 & 2 and then aliskiren on top of the max tolerated dose of enalapril for step 3. Patients who completed the run in were randomized in a 1:1:1 ratio to one of the 3 treatment arms (aliskiren/enalapril combination therapy, aliskiren monotherapy, or enalapril monotherapy).

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 | Investigator, Monitor, Carer, Subject, Data analyst, Assessor |

Arms

| | |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Combination Aliskiren / Enalapril |

Arm description:

Aliskiren / Enalapril combination therapy-150 mg/10 mg titrated to 300 mg/ 10 mg film-coated tablets and administered orally.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Aliskiren |
| Investigational medicinal product code | SPP100 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Aliskiren 150 mg titrated to 300 mg oral film-coated tablet daily.

| | |
|--|--------------------|
| Investigational medicinal product name | Enalapril |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Enalapril 10 mg oral film-coated tablet daily.

| | |
|------------------|-----------|
| Arm title | Aliskiren |
|------------------|-----------|

Arm description:

Aliskiren monotherapy - 150 mg titrated to 300 mg film-coated tablets and administered orally.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Aliskiren |
| Investigational medicinal product code | SPP100 |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Aliskiren 150 mg titrated to 300 mg oral film-coated tablet daily.

| | |
|------------------|-----------|
| Arm title | Enalapril |
|------------------|-----------|

Arm description:

Enalapril monotherapy -10 mg film-coated tablet and administered orally.

| | |
|--|--------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Enalapril |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Enalapril 10 mg oral film-coated tablet daily.

| Number of subjects in period 1 | Combination Aliskiren / Enalapril | Aliskiren | Enalapril |
|---|--------------------------------------|-----------|-----------|
| Started | 2354 | 2356 | 2354 |
| Full Analysis Set (FAS) | 2340 | 2340 | 2336 |
| Safety Set | 2347 | 2348 | 2345 |
| Completed | 1567 | 1524 | 1539 |
| Not completed | 787 | 832 | 815 |
| Vital Status known (alive) at study end | 2 | 3 | 3 |
| Death | 713 | 768 | 753 |
| H.A. Request | 26 | 23 | 19 |
| Vital Status at study end N/A | 8 | 10 | 10 |
| IRB request | - | - | 2 |
| Lost to follow-up | 11 | 6 | 11 |
| Vital Status unknown at study end | 1 | 1 | - |
| Patient's request | 21 | 17 | 11 |
| Missing study completion information | 5 | 4 | 6 |

Baseline characteristics

Reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | Combination Aliskiren / Enalapril |
| Reporting group description: Aliskiren / Enalapril combination therapy-150 mg/10 mg titrated to 300 mg/ 10 mg film-coated tablets and administered orally. | |
| Reporting group title | Aliskiren |
| Reporting group description: Aliskiren monotherapy - 150 mg titrated to 300 mg film-coated tablets and administered orally. | |
| Reporting group title | Enalapril |
| Reporting group description: Enalapril monotherapy -10 mg film-coated tablet and administered orally. | |

| Reporting group values | Combination Aliskiren / Enalapril | Aliskiren | Enalapril |
|--|-----------------------------------|-----------|-----------|
| Number of subjects | 2354 | 2356 | 2354 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 1219 | 1185 | 1201 |
| From 65-84 years | 1099 | 1130 | 1128 |
| 85 years and over | 36 | 41 | 25 |
| Age Continuous Units: years | | | |
| arithmetic mean | 63.2 | 63.3 | 63.3 |
| standard deviation | ± 11.65 | ± 12.06 | ± 11.71 |
| Gender, Male/Female Units: Subjects | | | |
| Male | 1857 | 1822 | 1850 |
| Female | 497 | 534 | 504 |

| Reporting group values | Total | | |
|--|-------|--|--|
| Number of subjects | 7064 | | |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |

| | | | |
|---|------|--|--|
| Adults (18-64 years) | 3605 | | |
| From 65-84 years | 3357 | | |
| 85 years and over | 102 | | |
| Age Continuous Units: years arithmetic mean standard deviation | - | | |
| Gender, Male/Female Units: Subjects | | | |
| Male | 5529 | | |
| Female | 1535 | | |

End points

End points reporting groups

| | |
|---|-----------------------------------|
| Reporting group title | Combination Aliskiren / Enalapril |
| Reporting group description: Aliskiren / Enalapril combination therapy-150 mg/10 mg titrated to 300 mg/ 10 mg film-coated tablets and administered orally. | |
| Reporting group title | Aliskiren |
| Reporting group description: Aliskiren monotherapy - 150 mg titrated to 300 mg film-coated tablets and administered orally. | |
| Reporting group title | Enalapril |
| Reporting group description: Enalapril monotherapy -10 mg film-coated tablet and administered orally. | |

Primary: Number of participants that had first occurrence of the composite endpoint, which is defined as either Cardiovascular (CV) death or Heart Failure (HF) hospitalization

| | |
|--|--|
| End point title | Number of participants that had first occurrence of the composite endpoint, which is defined as either Cardiovascular (CV) death or Heart Failure (HF) hospitalization |
| End point description: Number of participants that had first occurrence of the composite endpoint, which is defined as either CV death or HF hospitalization due to HF. | |
| End point type | Primary |
| End point timeframe: up to End of Study (78 months) | |

| End point values | Combination Aliskiren / Enalapril | Aliskiren | Enalapril | |
|-----------------------------|-----------------------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2340 | 2340 | 2336 | |
| Units: participants | | | | |
| Primary Composite | 770 | 791 | 808 | |
| CV death | 512 | 562 | 547 | |
| 1st HF Hospitalization | 430 | 442 | 452 | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Superiority Statistical Analysis |
| Statistical analysis description: Superiority of Combination Aliskiren / Enalapril versus Enalapril monotherapy | |
| Comparison groups | Combination Aliskiren / Enalapril v Enalapril |

| | |
|---|-------------------|
| Number of subjects included in analysis | 4676 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1724 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 1.03 |

| | |
|---|---|
| Statistical analysis title | Superiority Non-Diabetic patients |
| Statistical analysis description: | |
| Superiority of Combination Aliskiren / Enalapril versus Enalapril monotherapy Non-Diabetic patients | |
| Comparison groups | Combination Aliskiren / Enalapril v Enalapril |
| Number of subjects included in analysis | 4676 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4579 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.96 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 1.07 |

| | |
|--|--------------------------------------|
| Statistical analysis title | Non-Inferiority Statistical Analysis |
| Statistical analysis description: | |
| Non-Inferiority Statistical Analysis of Aliskiren monotherapy versus Enalapril monotherapy | |
| Comparison groups | Aliskiren v Enalapril |
| Number of subjects included in analysis | 4676 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| P-value | = 0.0368 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.1 |

Notes:

[1] - Pre-specified Non-inferiority margin 1.104 is used.

| | |
|---|----------------------------------|
| Statistical analysis title | Superiority Statistical Analysis |
| Statistical analysis description: Superiority Statistical Analysis of Aliskiren monotherapy versus Enalapril monotherapy | |
| Comparison groups | Aliskiren v Enalapril |
| Number of subjects included in analysis | 4676 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9118 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.1 |

Secondary: Change from baseline to Month 12 for the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score

| | |
|---|---|
| End point title | Change from baseline to Month 12 for the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score |
| End point description: Change from baseline to Month 12 for the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score. KCCQ is a 23-item, self-administered instrument that quantifies physical function, symptoms (frequency, severity and recent change), social function, self-efficacy and knowledge, and quality of life. KCCQ clinical summary score is a composite assessment of physical limitations and total symptom scores. Scores are transformed to a range of 0-100, in which higher scores reflect better health status. | |
| End point type | Secondary |
| End point timeframe: Baseline, Month 12 | |

| End point values | Combination Aliskiren / Enalapril | Aliskiren | Enalapril | |
|-------------------------------------|-----------------------------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2340 | 2340 | 2336 | |
| Units: KCCQ Score | | | | |
| least squares mean (standard error) | -5.04 (± 0.56) | -6.03 (± 0.57) | -5.01 (± 0.55) | |

Statistical analyses

No statistical analyses for this end point

Secondary: All Cause Death

| | |
|-----------------|-----------------|
| End point title | All Cause Death |
|-----------------|-----------------|

End point description:

Number of patients - All-cause death. All-cause death is common in Heart Failure HF patients this measures how many patients had this event.

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

End point timeframe:

up to end of study (78 months)

| End point values | Combination Aliskiren / Enalapril | Aliskiren | Enalapril | |
|-----------------------------|---|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 2340 | 2340 | 2336 | |
| Units: participants | 595 | 654 | 646 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Combination |
|-----------------------|-------------|

Reporting group description:

Combination

| | |
|-----------------------|-----------|
| Reporting group title | Aliskiren |
|-----------------------|-----------|

Reporting group description:

Aliskiren

| | |
|-----------------------|-----------|
| Reporting group title | Enalapril |
|-----------------------|-----------|

Reporting group description:

Enalapril

| Serious adverse events | Combination | Aliskiren | Enalapril |
|---|-------------------------|-------------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1466 / 2347 (62.46%) | 1504 / 2348 (64.05%) | 1501 / 2345 (64.01%) |
| number of deaths (all causes) | 349 | 403 | 392 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma gastric | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma of appendix | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 8 / 2348 (0.34%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 9 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal adenoma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 5 / 2348 (0.21%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign ear neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign lung neoplasm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign neoplasm of bladder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign neoplasm of skin | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign neoplasm of spinal cord | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign neoplasm of thyroid gland | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign pancreatic neoplasm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign renal neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign salivary gland neoplasm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct adenocarcinoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder cancer | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 4 / 2348 (0.17%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder cancer recurrent | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder papilloma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone cancer | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain neoplasm malignant | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cancer female | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial carcinoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 7 / 2345 (0.30%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carcinoma in situ of penis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carcinoma in situ of skin | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac valve fibroelastoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar tumour | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic lymphocytic leukaemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon adenoma | | | |

| | | | |
|--|-------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer | | | |
| subjects affected / exposed | 10 / 2347 (0.43%) | 4 / 2348 (0.17%) | 7 / 2345 (0.30%) |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 4 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon cancer recurrent | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal cancer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extranodal marginal zone B-cell lymphoma (MALT type) | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gallbladder cancer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric adenoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric cancer | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal cancer metastatic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal carcinoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glioblastoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glioma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemangioma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cancer | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cancer metastatic | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypopharyngeal cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected neoplasm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive ductal breast carcinoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Keratoacanthoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine benign neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal cancer | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lentigo maligna | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lip and/or oral cavity cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lip neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lipoma | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung adenocarcinoma metastatic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung carcinoma cell type unspecified stage IV | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 9 / 2348 (0.38%) | 12 / 2345 (0.51%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |

| | | | |
|--|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm of auricular cartilage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm of renal pelvis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant palate neoplasm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant pleural effusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mediastinum neoplasm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningioma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningioma benign | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to bone | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to bone marrow | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to liver | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 7 / 2348 (0.30%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to lung | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to lymph nodes | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to peritoneum | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to pleura | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to spine | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic pain | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myeloproliferative disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngeal cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasm malignant | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuroendocrine carcinoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-small cell lung cancer stage IV | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal carcinoma | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic carcinoma metastatic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic carcinoma stage IV | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Penile cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pineal parenchymal neoplasm malignant | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural mesothelioma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 7 / 2348 (0.30%) | 19 / 2345 (0.81%) |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 8 | 0 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer metastatic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatic adenoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal cancer | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectosigmoid cancer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cancer | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cancer metastatic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal neoplasm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salivary gland adenoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus cancer metastatic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin cancer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small cell lung cancer recurrent | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid cancer | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid neoplasm | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tongue neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour flare | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour pain | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine cancer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Accelerated hypertension | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 5 / 2347 (0.21%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aneurysm ruptured | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 8 / 2348 (0.34%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 8 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic aneurysm rupture | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic arteriosclerosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic dilatation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic dissection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic rupture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic stenosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic thrombosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arterial insufficiency | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arterial stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arterial thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriovenous fistula | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteritis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bleeding varicose vein | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Circulatory collapse | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 2 / 7 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 5 / 2348 (0.21%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic vascular disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism arterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism venous | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extremity necrosis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral artery embolism | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral artery occlusion | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 1 / 2348 (0.04%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemodynamic instability | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 17 / 2347 (0.72%) | 13 / 2348 (0.55%) | 10 / 2345 (0.43%) |
| occurrences causally related to treatment / all | 0 / 19 | 1 / 13 | 0 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive crisis | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive emergency | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 37 / 2347 (1.58%) | 49 / 2348 (2.09%) | 26 / 2345 (1.11%) |
| occurrences causally related to treatment / all | 9 / 38 | 18 / 52 | 9 / 34 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iliac artery embolism | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iliac artery occlusion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intermittent claudication | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 5 / 2348 (0.21%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic limb pain | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 3 / 2348 (0.13%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 1 / 5 | 1 / 3 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 18 / 2347 (0.77%) | 13 / 2348 (0.55%) | 11 / 2345 (0.47%) |
| occurrences causally related to treatment / all | 0 / 22 | 0 / 15 | 0 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral artery aneurysm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral artery stenosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 5 / 2347 (0.21%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral embolism | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 8 / 2348 (0.34%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 9 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral vascular disorder | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral venous disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 4 / 2348 (0.17%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post thrombotic syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Secondary hypertension | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subclavian artery stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicophlebitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicose ulceration | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicose vein | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular rupture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venous haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venous thrombosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Heart transplant | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Abasia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-------------------|-------------------|-------------------|
| Accidental death | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 8 / 2347 (0.34%) | 5 / 2348 (0.21%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain death | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac complication associated with device | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac death | | | |
| subjects affected / exposed | 51 / 2347 (2.17%) | 68 / 2348 (2.90%) | 87 / 2345 (3.71%) |
| occurrences causally related to treatment / all | 0 / 51 | 1 / 68 | 1 / 87 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 75 / 2347 (3.20%) | 84 / 2348 (3.58%) | 82 / 2345 (3.50%) |
| occurrences causally related to treatment / all | 1 / 75 | 0 / 84 | 0 / 82 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device battery issue | | | |

| | | | |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed | 13 / 2347 (0.55%) | 9 / 2348 (0.38%) | 14 / 2345 (0.60%) |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 9 | 0 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device breakage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device defective | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device electrical impedance issue | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device end of service | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device failure | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device inappropriate shock delivery | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device issue | | | |

| | | | |
|---|------------------|-------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device lead damage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device lead issue | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device malfunction | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 10 / 2348 (0.43%) | 9 / 2345 (0.38%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 10 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device signal detection issue | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device stimulation issue | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disease progression | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exercise tolerance decreased | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 5 | 1 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Feeling abnormal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 3 / 2348 (0.13%) | 7 / 2345 (0.30%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hernia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypothermia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ill-defined disorder | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site erosion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site haemorrhage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site necrosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site pain | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site ulcer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incarcerated hernia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inflammation | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury associated with device | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lead dislodgement | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised oedema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 4 / 2348 (0.17%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device complication | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device site thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metaplasia | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multi-organ failure | | | |
| subjects affected / exposed | 21 / 2347 (0.89%) | 15 / 2348 (0.64%) | 12 / 2345 (0.51%) |
| occurrences causally related to treatment / all | 0 / 21 | 0 / 15 | 0 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 13 / 2347 (0.55%) | 15 / 2348 (0.64%) | 22 / 2345 (0.94%) |
| occurrences causally related to treatment / all | 0 / 15 | 0 / 16 | 0 / 24 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 6 / 2348 (0.26%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 13 | 1 / 7 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Organ failure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 5 / 2347 (0.21%) | 8 / 2348 (0.34%) | 7 / 2345 (0.30%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 9 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stent-graft endoleak | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden cardiac death | | | |
| subjects affected / exposed | 38 / 2347 (1.62%) | 39 / 2348 (1.66%) | 50 / 2345 (2.13%) |
| occurrences causally related to treatment / all | 2 / 38 | 5 / 39 | 3 / 50 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 98 / 2347 (4.18%) | 89 / 2348 (3.79%) | 86 / 2345 (3.67%) |
| occurrences causally related to treatment / all | 0 / 98 | 0 / 89 | 1 / 86 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosis in device | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulcer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Undersensing | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular stent restenosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular stent stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular stent thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Allergy to venom | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactic shock | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heart transplant rejection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transplant rejection | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| Immobile | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Treatment noncompliance | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Acquired hydrocele | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 9 / 2348 (0.38%) | 7 / 2345 (0.30%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast hyperplasia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mammary fistula | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|------------------|
| Metrorrhagia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postmenopausal haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatic obstruction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatomegaly | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectocele | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scrotal oedema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spermatocele | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine polyp | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 20 / 2347 (0.85%) | 20 / 2348 (0.85%) | 17 / 2345 (0.72%) |
| occurrences causally related to treatment / all | 0 / 24 | 2 / 25 | 0 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 13 / 2347 (0.55%) | 8 / 2348 (0.34%) | 14 / 2345 (0.60%) |
| occurrences causally related to treatment / all | 0 / 15 | 0 / 12 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alveolitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Apnoea | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asphyxia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 4 / 2347 (0.17%) | 8 / 2348 (0.34%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 11 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthmatic crisis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiectasis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis chronic | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopleural fistula | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchospasm | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cheyne-Stokes respiration | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 32 / 2347 (1.36%) | 32 / 2348 (1.36%) | 43 / 2345 (1.83%) |
| occurrences causally related to treatment / all | 0 / 42 | 1 / 41 | 0 / 60 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic respiratory failure | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cough | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diaphragmatic paralysis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 54 / 2347 (2.30%) | 46 / 2348 (1.96%) | 35 / 2345 (1.49%) |
| occurrences causally related to treatment / all | 0 / 65 | 0 / 59 | 0 / 45 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea at rest | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Emphysema | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 4 / 2347 (0.17%) | 3 / 2348 (0.13%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemothorax | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiccups | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrothorax | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercapnia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperventilation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Idiopathic pulmonary fibrosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal oedema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasal septum deviation | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Organising pneumonia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oropharyngeal pain | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthopnoea | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngeal oedema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 10 / 2347 (0.43%) | 11 / 2348 (0.47%) | 12 / 2345 (0.51%) |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 13 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleurisy | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleurocutaneous fistula | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumomediastinum | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 6 / 2348 (0.26%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 6 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax spontaneous | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary alveolar haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary artery thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 17 / 2347 (0.72%) | 18 / 2348 (0.77%) | 9 / 2345 (0.38%) |
| occurrences causally related to treatment / all | 0 / 18 | 0 / 18 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary haematoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 4 / 2348 (0.17%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary mass | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 27 / 2347 (1.15%) | 27 / 2348 (1.15%) | 14 / 2345 (0.60%) |
| occurrences causally related to treatment / all | 0 / 37 | 0 / 30 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary venous thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory arrest | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 16 / 2347 (0.68%) | 16 / 2348 (0.68%) | 26 / 2345 (1.11%) |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 16 | 2 / 28 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Snoring | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suffocation feeling | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vocal cord leukoplakia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Abulia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute psychosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adjustment disorder | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcohol abuse | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcoholism | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anxiety | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anxiety disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Apathy | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bipolar disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Catatonia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Completed suicide | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Confusional state | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Delirium | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Delusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 6 / 2348 (0.26%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disorientation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fear | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Insomnia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Major depression | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mood disorder due to a general medical condition | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Restlessness | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Schizophrenia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Somatisation disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct obstruction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct stenosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct stone | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary cirrhosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary colic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary dilatation | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 5 / 2348 (0.21%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis acute | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 4 / 2348 (0.17%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 9 / 2348 (0.38%) | 9 / 2345 (0.38%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |
| subjects affected / exposed | 18 / 2347 (0.77%) | 15 / 2348 (0.64%) | 13 / 2345 (0.55%) |
| occurrences causally related to treatment / all | 1 / 18 | 0 / 15 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic hepatitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cirrhosis alcoholic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic congestion | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic steatosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis acute | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis alcoholic | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatorenal failure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatorenal syndrome | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperbilirubinaemia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic hepatitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice hepatocellular | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-alcoholic steatohepatitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Portal hypertension | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Anticoagulation drug level below therapeutic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anticoagulation drug level increased | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 4 / 2348 (0.17%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 1 / 8 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood ethanol increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood magnesium decreased | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood urine | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood urine present | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac output decreased | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardioactive drug level increased | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest X-ray abnormal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coagulation test abnormal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coagulation time prolonged | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ejection fraction abnormal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram QRS complex prolonged | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterobacter test positive | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heart rate decreased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heart rate irregular | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| International normalised ratio abnormal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 3 / 2348 (0.13%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oxygen saturation decreased | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatic specific antigen increased | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urine output decreased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral load increased | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Accident | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Accidental exposure to product | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acetabulum fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcohol poisoning | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anastomotic complication | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anastomotic ulcer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 4 / 2348 (0.17%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Avulsion fracture | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone contusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain contusion | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Burns third degree | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carbon monoxide poisoning | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac function disturbance postoperative | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac procedure complication | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carotid artery restenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical vertebral fracture | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest injury | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clavicle fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Closed globe injury | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Comminuted fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Complications of transplanted heart | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contusion | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery reocclusion | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery restenosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary vascular graft occlusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Craniocerebral injury | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Excoriation | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extradural haematoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial bones fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 8 / 2348 (0.34%) | 11 / 2345 (0.47%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |

| | | | |
|---|------------------|-------------------|------------------|
| subjects affected / exposed | 5 / 2347 (0.21%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 10 / 2348 (0.43%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 11 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign body | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture displacement | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fractured ischium | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fractured sacrum | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head injury | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 5 / 2348 (0.21%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision site haematoma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal anastomosis complication | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ligament injury | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb traumatic amputation | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lip injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniscus injury | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mouth injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple fractures | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple injuries | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle injury | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle rupture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 9 / 2348 (0.38%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 9 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Patella fracture | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic fracture | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periorbital haemorrhage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral artery restenosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periprosthetic fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax traumatic | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Poisoning | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural bile leak | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haematoma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haematuria | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post-traumatic pain | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative hernia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative ileus | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative thoracic procedure complication | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound complication | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural complication | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product name confusion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pubis fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary contusion | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radius fracture | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 5 / 2348 (0.21%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory fume inhalation disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | | | |
| subjects affected / exposed | 8 / 2347 (0.34%) | 6 / 2348 (0.26%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 6 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sacroiliac fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scrotal haematoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shunt stenosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin abrasion | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 5 / 2348 (0.21%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haemorrhage | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon rupture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thermal burn | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transplant failure | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic fracture | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic haematoma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic haemothorax | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic intracranial haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic liver injury | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic shock | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ulna fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Underdose | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethral stricture traumatic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular bypass dysfunction | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular graft occlusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular pseudoaneurysm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasoplegia syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermoid cyst | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 18 / 2348 (0.77%) | 16 / 2345 (0.68%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 19 | 0 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute left ventricular failure | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 5 / 2348 (0.21%) | 9 / 2345 (0.38%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 49 / 2347 (2.09%) | 40 / 2348 (1.70%) | 46 / 2345 (1.96%) |
| occurrences causally related to treatment / all | 0 / 50 | 1 / 41 | 1 / 47 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adams-Stokes syndrome | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |
| subjects affected / exposed | 35 / 2347 (1.49%) | 33 / 2348 (1.41%) | 37 / 2345 (1.58%) |
| occurrences causally related to treatment / all | 0 / 41 | 1 / 39 | 1 / 51 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 47 / 2347 (2.00%) | 48 / 2348 (2.04%) | 41 / 2345 (1.75%) |
| occurrences causally related to treatment / all | 0 / 68 | 0 / 54 | 0 / 49 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic valve disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arrhythmia | | | |
| subjects affected / exposed | 13 / 2347 (0.55%) | 15 / 2348 (0.64%) | 12 / 2345 (0.51%) |
| occurrences causally related to treatment / all | 1 / 13 | 0 / 17 | 0 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 89 / 2347 (3.79%) | 98 / 2348 (4.17%) | 97 / 2345 (4.14%) |
| occurrences causally related to treatment / all | 0 / 105 | 1 / 120 | 0 / 118 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 15 / 2347 (0.64%) | 21 / 2348 (0.89%) | 11 / 2345 (0.47%) |
| occurrences causally related to treatment / all | 1 / 17 | 0 / 25 | 0 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial tachycardia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 8 / 2348 (0.34%) | 13 / 2345 (0.55%) |
| occurrences causally related to treatment / all | 0 / 7 | 1 / 8 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block first degree | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 4 / 2348 (0.17%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bifascicular block | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bradyarrhythmia | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bradycardia | | | |
| subjects affected / exposed | 12 / 2347 (0.51%) | 12 / 2348 (0.51%) | 9 / 2345 (0.38%) |
| occurrences causally related to treatment / all | 0 / 12 | 2 / 13 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bundle branch block | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bundle branch block left | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac aneurysm | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 59 / 2347 (2.51%) | 61 / 2348 (2.60%) | 59 / 2345 (2.52%) |
| occurrences causally related to treatment / all | 0 / 63 | 0 / 63 | 3 / 62 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac asthma | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 4 / 2348 (0.17%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac discomfort | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorder | | | |

| | | | |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 480 / 2347 (20.45%) | 521 / 2348 (22.19%) | 503 / 2345 (21.45%) |
| occurrences causally related to treatment / all | 15 / 892 | 17 / 996 | 20 / 903 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 54 / 2347 (2.30%) | 43 / 2348 (1.83%) | 60 / 2345 (2.56%) |
| occurrences causally related to treatment / all | 1 / 75 | 1 / 56 | 2 / 80 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 120 / 2347 (5.11%) | 125 / 2348 (5.32%) | 122 / 2345 (5.20%) |
| occurrences causally related to treatment / all | 3 / 209 | 3 / 189 | 8 / 220 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 76 / 2347 (3.24%) | 85 / 2348 (3.62%) | 79 / 2345 (3.37%) |
| occurrences causally related to treatment / all | 3 / 123 | 4 / 136 | 1 / 140 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac flutter | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac hypertrophy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac perforation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac sarcoidosis | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac valve disease | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac ventricular thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 24 / 2347 (1.02%) | 24 / 2348 (1.02%) | 20 / 2345 (0.85%) |
| occurrences causally related to treatment / all | 1 / 24 | 3 / 24 | 0 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 31 / 2347 (1.32%) | 49 / 2348 (2.09%) | 38 / 2345 (1.62%) |
| occurrences causally related to treatment / all | 1 / 32 | 2 / 52 | 0 / 44 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiomegaly | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary failure | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 4 / 2347 (0.17%) | 6 / 2348 (0.26%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 6 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiorenal syndrome | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiovascular disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiovascular insufficiency | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chordae tendinae rupture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronotropic incompetence | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 14 / 2347 (0.60%) | 14 / 2348 (0.60%) | 19 / 2345 (0.81%) |
| occurrences causally related to treatment / all | 0 / 15 | 0 / 14 | 0 / 22 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 28 / 2347 (1.19%) | 27 / 2348 (1.15%) | 22 / 2345 (0.94%) |
| occurrences causally related to treatment / all | 0 / 31 | 1 / 29 | 0 / 25 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery insufficiency | | | |

| | | | |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 8 / 2347 (0.34%) | 5 / 2348 (0.21%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 7 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extrasystoles | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heart valve incompetence | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive heart disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic cardiomyopathy | | | |
| subjects affected / exposed | 13 / 2347 (0.55%) | 7 / 2348 (0.30%) | 13 / 2345 (0.55%) |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 8 | 0 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Left ventricular dysfunction | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 6 / 2347 (0.26%) | 6 / 2348 (0.26%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Left ventricular failure | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 5 / 2348 (0.21%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 7 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic cardiomyopathy | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 17 / 2348 (0.72%) | 14 / 2345 (0.60%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 19 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mitral valve prolapse | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mitral valve stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 56 / 2347 (2.39%) | 50 / 2348 (2.13%) | 50 / 2345 (2.13%) |
| occurrences causally related to treatment / all | 1 / 63 | 0 / 51 | 0 / 57 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 19 / 2347 (0.81%) | 19 / 2348 (0.81%) | 18 / 2345 (0.77%) |
| occurrences causally related to treatment / all | 0 / 20 | 1 / 19 | 0 / 21 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nodal rhythm | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Papillary muscle rupture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary valve incompetence | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Restrictive cardiomyopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhythm idioventricular | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinoatrial block | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus arrhythmia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 3 / 2348 (0.13%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 6 | 1 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachyarrhythmia | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |

| | | | |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed | 7 / 2347 (0.30%) | 5 / 2348 (0.21%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 5 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systolic dysfunction | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachyarrhythmia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 5 / 2348 (0.21%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 1 / 10 | 0 / 5 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia paroxysmal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tricuspid valve disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tricuspid valve incompetence | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 14 / 2347 (0.60%) | 8 / 2348 (0.34%) | 14 / 2345 (0.60%) |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 8 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular dysfunction | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular dyssynchrony | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 8 / 2347 (0.34%) | 9 / 2348 (0.38%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 1 / 8 | 0 / 9 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular failure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 32 / 2347 (1.36%) | 30 / 2348 (1.28%) | 34 / 2345 (1.45%) |
| occurrences causally related to treatment / all | 2 / 33 | 2 / 33 | 1 / 37 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular flutter | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachyarrhythmia | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 78 / 2347 (3.32%) | 67 / 2348 (2.85%) | 63 / 2345 (2.69%) |
| occurrences causally related to treatment / all | 2 / 97 | 2 / 92 | 0 / 75 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Ageusia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Altered state of consciousness | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amyotrophic lateral sclerosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aphasia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atonic seizures | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basilar artery stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain hypoxia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain injury | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain stem infarction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain stem syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carotid arteriosclerosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carotid artery disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 5 / 2348 (0.21%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar ataxia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar infarction | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral amyloid angiopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral arteriosclerosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral artery embolism | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral artery occlusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral atrophy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haematoma | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 9 / 2348 (0.38%) | 7 / 2345 (0.30%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 9 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral infarction | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 17 / 2348 (0.72%) | 17 / 2345 (0.72%) |
| occurrences causally related to treatment / all | 0 / 10 | 1 / 17 | 0 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 44 / 2347 (1.87%) | 51 / 2348 (2.17%) | 62 / 2345 (2.64%) |
| occurrences causally related to treatment / all | 1 / 48 | 0 / 53 | 2 / 69 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular insufficiency | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervicogenic headache | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cognitive disorder | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Complex partial seizures | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dementia | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic coma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic hyperosmolar coma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |

| | | | |
|---|-------------------|------------------|------------------|
| subjects affected / exposed | 11 / 2347 (0.47%) | 9 / 2348 (0.38%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 1 / 11 | 0 / 10 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness postural | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysarthria | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyslalia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic cerebral infarction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalomalacia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 7 / 2348 (0.30%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 4 / 2348 (0.17%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemianopia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemianopia homonymous | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiplegia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocephalus | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemic coma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemic seizure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxic-ischaemic encephalopathy | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| IIIrd nerve paresis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intraventricular haemorrhage | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 45 / 2347 (1.92%) | 45 / 2348 (1.92%) | 29 / 2345 (1.24%) |
| occurrences causally related to treatment / all | 1 / 47 | 0 / 51 | 0 / 30 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lacunar infarction | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukoencephalopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 3 / 2348 (0.13%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 5 | 1 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental retardation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Monoparesis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Monoplegia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Motor neurone disease | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myoclonus | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Narcolepsy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic intolerance | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraesthesia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraparesis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paresis cranial nerve | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parkinson's disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parkinsonism | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Partial seizures | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postresuscitation encephalopathy | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Presyncope | | | |

| | | | |
|--|------------------|------------------|------------------|
| subjects affected / exposed | 4 / 2347 (0.17%) | 5 / 2348 (0.21%) | 9 / 2345 (0.38%) |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 5 | 1 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radiculopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retrograde amnesia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reversible ischaemic neurological deficit | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Somnolence | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal epidural haematoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 48 / 2347 (2.05%) | 56 / 2348 (2.39%) | 27 / 2345 (1.15%) |
| occurrences causally related to treatment / all | 5 / 58 | 7 / 71 | 1 / 31 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tension headache | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thalamus haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient global amnesia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 23 / 2347 (0.98%) | 20 / 2348 (0.85%) | 15 / 2345 (0.64%) |
| occurrences causally related to treatment / all | 0 / 23 | 0 / 20 | 1 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Trigeminal nerve disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uraemic encephalopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VIIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular dementia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular encephalopathy | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertebrobasilar insufficiency | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Acquired haemophilia | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 36 / 2347 (1.53%) | 28 / 2348 (1.19%) | 28 / 2345 (1.19%) |
| occurrences causally related to treatment / all | 2 / 39 | 0 / 40 | 1 / 31 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia vitamin B12 deficiency | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aplastic anaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bicytopenia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone marrow infiltration | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic diathesis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypochromic anaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocoagulable state | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice acholuric | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenopathy mediastinal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Microcytic anaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polycythaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retroperitoneal lymphadenopathy | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic embolism | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic infarction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Deafness neurosensory | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deafness unilateral | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematotympanum | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meniere's disease | | | |

| | | | |
|---|-------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden hearing loss | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertigo | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertigo positional | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Amaurosis fugax | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amblyopia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cataract | | | |
| subjects affected / exposed | 13 / 2347 (0.55%) | 8 / 2348 (0.34%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 9 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Conjunctival haemorrhage | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic retinopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glaucoma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Macular hole | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ocular fistula | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ocular retrobulbar haemorrhage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ophthalmic vein thrombosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal artery embolism | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal artery occlusion | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal degeneration | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal vein occlusion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Visual acuity reduced | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal adhesions | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal hernia | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 14 / 2347 (0.60%) | 10 / 2348 (0.43%) | 11 / 2345 (0.47%) |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 23 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 5 / 2348 (0.21%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal strangulated hernia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal wall haematoma | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acid peptic disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute abdomen | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcoholic pancreatitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal fistula | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal prolapse | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 6 / 2348 (0.26%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 6 | 0 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune pancreatitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic gastritis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 5 / 2348 (0.21%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 5 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic gastroparesis | | | |

| | | | |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 18 / 2347 (0.77%) | 4 / 2348 (0.17%) | 11 / 2345 (0.47%) |
| occurrences causally related to treatment / all | 1 / 20 | 0 / 4 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dieulafoy's vascular malformation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticular perforation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum intestinal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulum intestinal haemorrhagic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer haemorrhage | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer perforation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterovesical fistula | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eosinophilic oesophagitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erosive duodenitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Faecaloma | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral hernia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral hernia, obstructive | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric polyps | | | |

| | | | |
|---|-------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 4 / 2348 (0.17%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 2 / 2348 (0.09%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer perforation | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 10 / 2347 (0.43%) | 4 / 2348 (0.17%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroduodenal ulcer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal angiodysplasia | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 19 / 2347 (0.81%) | 13 / 2348 (0.55%) | 11 / 2345 (0.47%) |
| occurrences causally related to treatment / all | 0 / 19 | 1 / 14 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal ischaemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal polyp haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal ulcer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gingival bleeding | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematochezia | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhagic erosive gastritis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 5 / 2348 (0.21%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incarcerated inguinal hernia | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incarcerated umbilical hernia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 23 / 2347 (0.98%) | 21 / 2348 (0.89%) | 14 / 2345 (0.60%) |
| occurrences causally related to treatment / all | 1 / 23 | 0 / 21 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal fistula | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal infarction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal perforation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal polyp | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal strangulation | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine polyp | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 5 / 2348 (0.21%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mallory-Weiss syndrome | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Melaena | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 4 / 2348 (0.17%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mesenteric artery embolism | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mesenteric artery thrombosis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mesenteritis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 4 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstruction gastric | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedematous pancreatitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatic cyst | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 5 / 2347 (0.21%) | 4 / 2348 (0.17%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 5 / 2348 (0.21%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 1 / 9 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis chronic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis necrotising | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peptic ulcer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peptic ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peptic ulcer perforation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngo-oesophageal diverticulum | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Portal hypertensive gastropathy | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proctitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 5 / 2348 (0.21%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal polyp | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal prolapse | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stress ulcer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus | | | |

| | | | |
|---|------------------|-------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosis mesenteric vessel | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tongue oedema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth disorder | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical hernia | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 5 / 2348 (0.21%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 12 / 2348 (0.51%) | 7 / 2345 (0.30%) |
| occurrences causally related to treatment / all | 0 / 6 | 1 / 12 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Visceral congestion | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Volvulus | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Volvulus of small bowel | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 5 / 2348 (0.21%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acquired epidermolysis bullosa | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Actinic keratosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angioedema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis allergic | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic foot | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ulcer | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug eruption | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fungating wound | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Henoch-Schonlein purpura | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intertrigo | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lichen sclerosus | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuropathic ulcer | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peau d'orange | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Precancerous skin lesion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pruritus | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Purpura | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin necrosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 4 / 2348 (0.17%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic skin eruption | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 52 / 2347 (2.22%) | 29 / 2348 (1.24%) | 38 / 2345 (1.62%) |
| occurrences causally related to treatment / all | 12 / 60 | 5 / 31 | 1 / 41 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute prerenal failure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anuria | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Azotaemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus bladder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus ureteric | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus urethral | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus urinary | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 21 / 2347 (0.89%) | 10 / 2348 (0.43%) | 10 / 2345 (0.43%) |
| occurrences causally related to treatment / all | 6 / 24 | 0 / 10 | 3 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic nephropathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysuria | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glomerulonephritis membranous | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 6 / 2348 (0.26%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 6 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive nephropathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic nephropathy | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephritis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephropathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polyuria | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postrenal failure | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prerenal failure | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proteinuria | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal cyst | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal embolism | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 33 / 2347 (1.41%) | 26 / 2348 (1.11%) | 27 / 2345 (1.15%) |
| occurrences causally related to treatment / all | 6 / 34 | 4 / 26 | 4 / 29 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 34 / 2347 (1.45%) | 31 / 2348 (1.32%) | 33 / 2345 (1.41%) |
| occurrences causally related to treatment / all | 9 / 36 | 8 / 33 | 8 / 33 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal infarct | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal tubular necrosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteric fistula | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteric stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethral obstruction | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethral stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary bladder haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary bladder polyp | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 7 / 2348 (0.30%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 9 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinoma | | | |

| | | | |
|--|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 5 / 2348 (0.21%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 5 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 7 / 2348 (0.30%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyrotoxic crisis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic nodular goitre | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 3 / 2348 (0.13%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|------------------|
| Back pain | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervical spinal stenosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chondropathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Compartment syndrome | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Connective tissue inflammation | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Costochondritis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic amyotrophy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fistula | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture malunion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gouty arthritis | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 5 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemarthrosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint effusion | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint instability | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle atrophy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 5 / 2348 (0.21%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal stiffness | | | |

| | | | |
|---|------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myopathy | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myopathy toxic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myositis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 9 / 2347 (0.38%) | 12 / 2348 (0.51%) | 10 / 2345 (0.43%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 15 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteochondritis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteochondrosis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoporosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoporotic fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 3 / 2348 (0.13%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polyarthritis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rheumatic disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 4 / 2348 (0.17%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal column stenosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal deformity | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal osteoarthritis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal sepsis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess intestinal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess jaw | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess limb | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess oral | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acinetobacter infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendiceal abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 2 / 2348 (0.09%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis perforated | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis infective | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial diarrhoea | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial sepsis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary sepsis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone tuberculosis | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 22 / 2347 (0.94%) | 16 / 2348 (0.68%) | 11 / 2345 (0.47%) |
| occurrences causally related to treatment / all | 0 / 26 | 0 / 16 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis viral | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Burn infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis infective | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac valve abscess | | | |

| | | | |
|---|------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 9 / 2348 (0.38%) | 13 / 2345 (0.55%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 12 | 0 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis infective | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic sinusitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Corynebacterium infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 6 / 2347 (0.26%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 6 / 2348 (0.26%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 10 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related sepsis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic foot infection | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 0 / 2348 (0.00%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysentery | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Empyema | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 5 / 2348 (0.21%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis bacterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis staphylococcal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis infectious | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterococcal sepsis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epididymitis | | | |

| | | | |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 7 / 2348 (0.30%) | 10 / 2345 (0.43%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 7 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fungal oesophagitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gangrene | | | |
| subjects affected / exposed | 10 / 2347 (0.43%) | 3 / 2348 (0.13%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer helicobacter | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 13 / 2347 (0.55%) | 10 / 2348 (0.43%) | 16 / 2345 (0.68%) |
| occurrences causally related to treatment / all | 0 / 13 | 1 / 10 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis clostridial | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Genitourinary tract infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Groin abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| H1N1 influenza | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma infection | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemophilus sepsis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic infection bacterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis B | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis viral | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster cutaneous disseminated | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Human ehrlichiosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Implant site infection | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision site abscess | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision site infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected cyst | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected seroma | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected skin ulcer | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 2 / 2348 (0.09%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infectious colitis | | | |

| | | | |
|--|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 4 / 2348 (0.17%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intervertebral discitis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal sepsis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Klebsiella sepsis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver abscess | | | |

| | | | |
|---|-------------------|------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised infection | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 4 / 2348 (0.17%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 6 / 2348 (0.26%) | 9 / 2345 (0.38%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 7 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 10 / 2347 (0.43%) | 6 / 2348 (0.26%) | 13 / 2345 (0.55%) |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 9 | 0 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lyme disease | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucormycosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mycobacterial infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myiasis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orchitis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oropharyngitis fungal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parametritis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periodontitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 3 / 2348 (0.13%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumococcal sepsis | | | |

| | | | |
|---|--------------------|--------------------|--------------------|
| subjects affected / exposed | 2 / 2347 (0.09%) | 5 / 2348 (0.21%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 136 / 2347 (5.79%) | 145 / 2348 (6.18%) | 122 / 2345 (5.20%) |
| occurrences causally related to treatment / all | 1 / 164 | 0 / 176 | 0 / 146 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia escherichia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia haemophilus | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia influenzal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia mycoplasmal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pneumococcal | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural sepsis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostatic abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomembranous colitis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psoas abscess | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 8 / 2347 (0.34%) | 6 / 2348 (0.26%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 6 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 3 / 2348 (0.13%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis chronic | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 8 / 2347 (0.34%) | 15 / 2348 (0.64%) | 19 / 2345 (0.81%) |
| occurrences causally related to treatment / all | 1 / 8 | 0 / 19 | 0 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection fungal | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 14 / 2347 (0.60%) | 18 / 2348 (0.77%) | 12 / 2345 (0.51%) |
| occurrences causally related to treatment / all | 0 / 15 | 0 / 19 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic necrosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 13 / 2347 (0.55%) | 21 / 2348 (0.89%) | 13 / 2345 (0.55%) |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 21 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin bacterial infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcal endocarditis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis septic | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheitis | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheobronchitis | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 5 / 2348 (0.21%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 8 | 1 / 7 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 2347 (0.17%) | 5 / 2348 (0.21%) | 6 / 2345 (0.26%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethritis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 22 / 2347 (0.94%) | 21 / 2348 (0.89%) | 19 / 2345 (0.81%) |
| occurrences causally related to treatment / all | 0 / 25 | 0 / 22 | 0 / 19 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 5 / 2347 (0.21%) | 7 / 2348 (0.30%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 3 / 2348 (0.13%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral pericarditis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral vasculitis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection bacterial | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection staphylococcal | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound sepsis | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Acidosis | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cachexia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carbohydrate intolerance | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 6 / 2348 (0.26%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 9 | 2 / 6 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 27 / 2347 (1.15%) | 21 / 2348 (0.89%) | 14 / 2345 (0.60%) |
| occurrences causally related to treatment / all | 1 / 30 | 0 / 24 | 0 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 15 / 2347 (0.64%) | 16 / 2348 (0.68%) | 10 / 2345 (0.43%) |
| occurrences causally related to treatment / all | 1 / 16 | 0 / 16 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 7 / 2347 (0.30%) | 6 / 2348 (0.26%) | 4 / 2345 (0.17%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |

| | | | |
|---|-------------------|-------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 3 / 2347 (0.13%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid retention | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gout | | | |
| subjects affected / exposed | 11 / 2347 (0.47%) | 11 / 2348 (0.47%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 13 | 1 / 14 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 6 / 2347 (0.26%) | 1 / 2348 (0.04%) | 3 / 2345 (0.13%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 21 / 2347 (0.89%) | 13 / 2348 (0.55%) | 20 / 2345 (0.85%) |
| occurrences causally related to treatment / all | 12 / 22 | 6 / 14 | 11 / 22 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperosmolar hyperglycaemic state | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperosmolar state | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypervolaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |

| | | | |
|---|-------------------|-------------------|-------------------|
| subjects affected / exposed | 10 / 2347 (0.43%) | 5 / 2348 (0.21%) | 5 / 2345 (0.21%) |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 6 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 10 / 2347 (0.43%) | 12 / 2348 (0.51%) | 10 / 2345 (0.43%) |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 14 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 5 / 2347 (0.21%) | 7 / 2348 (0.30%) | 10 / 2345 (0.43%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 10 | 1 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypophagia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoproteinaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 2 / 2348 (0.09%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Insulin resistance | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iron deficiency | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 1 / 2348 (0.04%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ketoacidosis | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Marasmus | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 2 / 2347 (0.09%) | 0 / 2348 (0.00%) | 2 / 2345 (0.09%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic disorder | | | |
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mineral deficiency | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obesity | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 0 / 2348 (0.00%) | 0 / 2345 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polydipsia | | | |

| | | | |
|---|-------------------|-------------------|------------------|
| subjects affected / exposed | 0 / 2347 (0.00%) | 0 / 2348 (0.00%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 2347 (0.04%) | 1 / 2348 (0.04%) | 1 / 2345 (0.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 12 / 2347 (0.51%) | 10 / 2348 (0.43%) | 8 / 2345 (0.34%) |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 11 | 1 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Combination | Aliskiren | Enalapril |
|---|----------------------|----------------------|----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1548 / 2347 (65.96%) | 1446 / 2348 (61.58%) | 1458 / 2345 (62.17%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 188 / 2347 (8.01%) | 180 / 2348 (7.67%) | 137 / 2345 (5.84%) |
| occurrences (all) | 248 | 220 | 172 |
| Hypotension | | | |
| subjects affected / exposed | 409 / 2347 (17.43%) | 308 / 2348 (13.12%) | 332 / 2345 (14.16%) |
| occurrences (all) | 618 | 403 | 439 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 199 / 2347 (8.48%) | 238 / 2348 (10.14%) | 184 / 2345 (7.85%) |
| occurrences (all) | 235 | 292 | 220 |
| Cardiac failure | | | |
| subjects affected / exposed | 241 / 2347 (10.27%) | 254 / 2348 (10.82%) | 238 / 2345 (10.15%) |
| occurrences (all) | 349 | 359 | 362 |
| Nervous system disorders | | | |
| Dizziness | | | |

| | | | |
|--|-------------------------------|-------------------------------|-------------------------------|
| subjects affected / exposed occurrences (all) | 179 / 2347 (7.63%) 230 | 140 / 2348 (5.96%) 173 | 144 / 2345 (6.14%) 185 |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 124 / 2347 (5.28%) 141 | 115 / 2348 (4.90%) 120 | 111 / 2345 (4.73%) 118 |
| General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all) | 182 / 2347 (7.75%) 233 | 183 / 2348 (7.79%) 241 | 176 / 2345 (7.51%) 216 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 145 / 2347 (6.18%) 171 | 117 / 2348 (4.98%) 124 | 116 / 2345 (4.95%) 131 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 285 / 2347 (12.14%) 372 | 223 / 2348 (9.50%) 281 | 286 / 2345 (12.20%) 354 |
| Dyspnoea subjects affected / exposed occurrences (all) | 204 / 2347 (8.69%) 268 | 216 / 2348 (9.20%) 318 | 213 / 2345 (9.08%) 274 |
| Renal and urinary disorders Renal impairment subjects affected / exposed occurrences (all) | 414 / 2347 (17.64%) 564 | 298 / 2348 (12.69%) 381 | 328 / 2345 (13.99%) 451 |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 151 / 2347 (6.43%) 179 | 138 / 2348 (5.88%) 182 | 147 / 2345 (6.27%) 190 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 185 / 2347 (7.88%) 270 | 187 / 2348 (7.96%) 261 | 186 / 2345 (7.93%) 265 |
| Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all) | 469 / 2347 (19.98%) 717 | 283 / 2348 (12.05%) 387 | 350 / 2345 (14.93%) 481 |

| | | | |
|--|---------------------------|---------------------------|---------------------------|
| Hypokalaemia subjects affected / exposed occurrences (all) | 130 / 2347 (5.54%) 178 | 149 / 2348 (6.35%) 223 | 116 / 2345 (4.95%) 157 |
|--|---------------------------|---------------------------|---------------------------|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 20 January 2010 | Amendment 1: The rationale of this amendment was to evaluate a non-invasive technique (BPro™ device) to measure central aortic pressure (CAP) in a representative subset of patients with chronic heart failure (NYHA Class II – IV) from the ATMOSPHERE population |
| 29 October 2010 | Amendment 2: This protocol amendment mainly served to add the contraindication for itraconazole and to allow the assessment of NT-proBNP at screening instead of BNP. Contraindication of itraconazole was added according to RMP (Risk Management Plan) requirement as it was observed that exposure to aliskiren was increased by the coadministration of cyclosporine and itraconazole. Therefore, concomitant use of aliskiren with potent inhibitors of p-glycoprotein (Pgp) (such as cyclosporine and itraconazole) is not recommended. Inclusion of patients with increased N-terminal pro-brain natriuretic peptide (NT-proBNP) was allowed in addition to patients with increased brain natriuretic peptide (BNP) as it appeared that some sites had only the possibility to measure NT-proBNP but not BNP. |
| 30 March 2012 | Amendment 3: The rationale of this local protocol amendment, which was only applicable for Costa Rica, followed a request from the local ethics committee to monitor fasting plasma glucose and HbA1c levels in all patients during the course of the trial. |
| 30 April 2013 | Amendment 4: This protocol amendment followed the request made by the CTFG on behalf of the HAs from the EU member states, after the submission of the ASTRONAUT study FIR to the HAs. Based on these results, the CTFG requested on 12-Feb-2013 that in the EU member states participating to the study, study drug be discontinued in all patients enrolled in ATMOSPHERE who have diabetes (but patients were to remain in the study and be followed up until trial end according to the study protocol), and no new patients with diabetes were allowed to be enrolled in the trial. Novartis complied with this request and amended the protocol to implement these changes consistently, across all participating countries worldwide. Other changes included in this amendment were to change from BNP to NT-proBNP in the analysis, which has the same clinical meaning but has a better chemical stability. Further, the statistical section was updated particularly in regard to the inclusion of an additional hypothesis (aliskiren/enalapril combination compared to enalapril monotherapy in nondiabetic patients), censoring rules for the time to event analysis and refinement in secondary objectives. One of the two secondary objectives (to evaluate whether aliskiren monotherapy and/or the combination of aliskiren/enalapril is superior to enalapril monotherapy in reducing the BNP level from baseline to predefined timepoint) was removed. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported