



## Clinical trial results: Early treatment of Atrial fibrillation for Stroke prevention Trial (EAST) Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2010-021258-20          |
| Trial protocol           | DE DK NL CZ BE ES PL IT |
| Global end of trial date | 29 May 2020             |

### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 27 May 2022   |
| First version publication date    | 27 May 2022   |
| Summary attachment (see zip file) | Final study report - EAST - AFNET 4 - 2010-021258-20 (EAST_AFNET4_CSR_complete_final_signed_20210224.pdf) |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | EAST-AFNET 4 |
|-----------------------|--------------|

#### Additional study identifiers

|                                    |                |
|------------------------------------|----------------|
| ISRCTN number                      | ISRCTN04708680 |
| ClinicalTrials.gov id (NCT number) | NCT01288352    |
| WHO universal trial number (UTN)   | -              |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Kompetenznetz Vorhofflimmern e.V. (AFNET)   |
| Sponsor organisation address | Mendelstraße 11 , Münster, Germany, 48149   |
| Public contact               | Clinical Trials Information, Kompetenznetz Vorhofflimmern e.V. (AFNET), +49 251980 1340, info@kompetenznetz-vorhofflimmern.de |
| Scientific contact           | Clinical Trials Information, Kompetenznetz Vorhofflimmern e.V. (AFNET), +49 251980 1340, info@kompetenznetz-vorhofflimmern.de |

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:

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**Results analysis stage**

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|  |             |
|--|-------------|
| Analysis stage                                       | Final       |
| Date of interim/final analysis                       | 29 May 2020 |
| Is this the analysis of the primary completion data? | Yes         |
| Primary completion date                              | 29 May 2020 |
| Global end of trial reached?                         | Yes         |
| Global end of trial date                             | 29 May 2020 |
| Was the trial ended prematurely?                     | No          |

Notes:

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**General information about the trial**

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Main objective of the trial:

To test whether an early and comprehensive rhythm control therapy can prevent adverse cardiovascular outcomes in patients with atrial fibrillation (AF) compared to usual care.

Protection of trial subjects:

No IMP was in use.

Risk-Assessment regarding Covid-19-Pandemic: Due to End of Observation being set to 06.03.2020 and to collection of last FU information via postal questionnaires (no personal visits), the safety of study participants was not affected by the current pandemic.

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Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 15 June 2011 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Netherlands: 180    |
| Country: Number of subjects enrolled | Poland: 163         |
| Country: Number of subjects enrolled | Spain: 129          |
| Country: Number of subjects enrolled | Belgium: 143        |
| Country: Number of subjects enrolled | Czechia: 35         |
| Country: Number of subjects enrolled | Denmark: 53         |
| Country: Number of subjects enrolled | Germany: 1664       |
| Country: Number of subjects enrolled | Italy: 125          |
| Country: Number of subjects enrolled | United Kingdom: 248 |
| Country: Number of subjects enrolled | Switzerland: 46     |
| Country: Number of subjects enrolled | France: 3           |
| Worldwide total number of subjects   | 2789                |
| EEA total number of subjects         | 2495                |

Notes:

| <b>Subjects enrolled per age group</b>    |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 585  |
| From 65 to 84 years                       | 2127 |
| 85 years and over                         | 77   |

## Subject disposition

### Recruitment

Recruitment details:

We enrolled adults ( $\geq 18$  years of age) who had early AF (defined as atrial fibrillation diagnosed  $\leq 12$  months before enrolment) and who were older than 75 years of age, have had a previous transient ischemic attack (TIA) or stroke, or met two of the following criteria: age greater than 65 years, female sex, heart failure, hypertension, diabetes

### Pre-assignment

Screening details:

Recent onset AF, i.e. AF with known history of  $\leq 1$  year prior to random

Risk for stroke by EITHER

a) 1 of the following: age  $> 75$ , prior stroke or transient ischemic attack

OR

b) 2 of the following: hypertension, diabetes mell, left ventricular hypertrophy, age  $> 65$ , fem sex, peripheral artery dis, kidney dis, stable heart fail, s cor a di

### Period 1

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

### Arms

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

Arm description:

Patients will receive either catheter ablation, or adequate antiarrhythmic drug therapy at an early time point. The initial therapy will be decided by the local investigator. Upon recurrence of AF, both modalities will be combined.

|  |                                 |
|--|---------------------------------|
| Arm type                               | Experimental                    |
| Investigational medicinal product name | adequate antiarrhythmic therapy |
| Investigational medicinal product code |                                 |
| Other name                             |                                 |
| Pharmaceutical forms                   | Tablet                          |
| Routes of administration               | Oral use                        |

Dosage and administration details:

according instructions

In Germany, Denmark, and Switzerland antiarrhythmic drugs (amiodarone, dronedarone, flecainide and propafenone) are considered investigational drugs whereas in the other countries these are not considered investigational drugs.

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Usual care |
|------------------|------------|

Arm description:

conducted following the current ESC guidelines for AF treatment.

|   |                 |
|---|-----------------|
| Arm type  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| <b>Number of subjects in period 1</b> | Early treatment | Usual care |
|---------------------------------------|-----------------|------------|
| Started                               | 1395            | 1394       |
| Completed                             | 1395            | 1394       |

## Baseline characteristics

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Early treatment |
|-----------------------|-----------------|

Reporting group description:

Patients will receive either catheter ablation, or adequate antiarrhythmic drug therapy at an early time point. The initial therapy will be decided by the local investigator. Upon recurrence of AF, both modalities will be combined.

|                       |            |
|-----------------------|------------|
| Reporting group title | Usual care |
|-----------------------|------------|

Reporting group description:

conducted following the current ESC guidelines for AF treatment.

| Reporting group values                             | Early treatment | Usual care | Total |
|--|-----------------|------------|-------|
| Number of subjects                                 | 1395            | 1394       | 2789  |
| 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)                               | 306             | 279        | 585   |
| From 65-84 years                                   | 1045            | 1082       | 2127  |
| 85 years and over                                  | 44              | 33         | 77    |
| Gender categorical                                 |                 |            |       |
| Units: Subjects                                    |                 |            |       |
| Female   | 645             | 648        | 1293  |
| Male   | 750             | 746        | 1496  |

## End points

### End points reporting groups

|   |                 |
|---|-----------------|
| Reporting group title   | Early treatment |
| Reporting group description:<br>Patients will receive either catheter ablation, or adequate antiarrhythmic drug therapy at an early time point. The initial therapy will be decided by the local investigator. Upon recurrence of AF, both modalities will be combined. |                 |
| Reporting group title   | Usual care      |
| Reporting group description:<br>conducted following the current ESC guidelines for AF treatment.  |                 |

### Primary: First Primary Outcome

|                        |                       |
|------------------------|-----------------------|
| End point title        | First Primary Outcome |
| End point description: |                       |
| End point type         | Primary               |
| End point timeframe:   |                       |
| Overall trial          |                       |

| End point values            | Early treatment | Usual care      |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1395            | 1394            |  |  |
| Units: Incidences           | 249             | 316             |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Regression analysis 1st primary outcome |
| Comparison groups                       | Usual care v Early treatment            |
| Number of subjects included in analysis | 2789                                    |
| Analysis specification                  | Pre-specified                           |
| Analysis type                           | superiority                             |
| P-value                                 | = 0.004                                 |
| Method                                  | Regression, Cox                         |

### Primary: Cardio vascular Death

|                        |                       |
|------------------------|-----------------------|
| End point title        | Cardio vascular Death |
| End point description: |                       |
| End point type         | Primary               |

End point timeframe:

Overall trial

| End point values            | Early treatment | Usual care      |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1395            | 1394            |  |  |
| Units: Incidences           | 67              | 94              |  |  |

### Statistical analyses

| Statistical analysis title              | Regression analysis          |
|---|------------------------------|
| Comparison groups                       | Early treatment v Usual care |
| Number of subjects included in analysis | 2789                         |
| Analysis specification                  | Pre-specified                |
| Analysis type                           | superiority                  |
| P-value                                 | = 0.039                      |
| Method                                  | Regression, Cox              |

### Primary: Stroke

|                        |         |
|------------------------|---------|
| End point title        | Stroke  |
| End point description: |         |
| End point type         | Primary |
| End point timeframe:   |         |
| Overall Trial          |         |

| End point values            | Early treatment | Usual care      |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1395            | 1394            |  |  |
| Units: Incidences           | 40              | 62              |  |  |

### Statistical analyses

| Statistical analysis title | Regression analysis Stroke   |
|----------------------------|------------------------------|
| Comparison groups          | Early treatment v Usual care |



|   |                 |
|---|-----------------|
| Number of subjects included in analysis | 2789            |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority     |
| P-value                                 | = 0.035         |
| Method                                  | Regression, Cox |

### Primary: Worsening of Heart Failure

|                        |                            |
|------------------------|----------------------------|
| End point title        | Worsening of Heart Failure |
| End point description: |                            |
| End point type         | Primary                    |
| End point timeframe:   |                            |
| Overall trial          |                            |

| End point values            | Early treatment | Usual care      |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1395            | 1394            |  |  |
| Units: Incidences           | 139             | 169             |  |  |

### Statistical analyses

|   |                                   |
|---|-----------------------------------|
| <b>Statistical analysis title</b>       | Regression analysis heart Failure |
| Comparison groups                       | Early treatment v Usual care      |
| Number of subjects included in analysis | 2789                              |
| Analysis specification                  | Pre-specified                     |
| Analysis type                           | superiority                       |
| P-value                                 | = 0.073                           |
| Method                                  | Regression, Cox                   |

### Primary: Acute Coronary Syndrome

|                        |                         |
|------------------------|-------------------------|
| End point title        | Acute Coronary Syndrome |
| End point description: |                         |
| End point type         | Primary                 |
| End point timeframe:   |                         |
| Overall Trial          |                         |

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | Early treatment | Usual care      |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1395            | 1394            |  |  |
| Units: Incidences           | 53              | 65              |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Regression analysis Corobary Heart Syndrome |
| Comparison groups                       | Early treatment v Usual care                |
| Number of subjects included in analysis | 2789  |
| Analysis specification                  | Pre-specified                               |
| Analysis type                           | superiority                                 |
| P-value                                 | = 0.309                                     |
| Method                                  | Regression, Cox                             |

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

|                       |                      |
|-----------------------|----------------------|
| Reporting group title | Early rhythm control |
|-----------------------|----------------------|

Reporting group description: -

|                       |            |
|-----------------------|------------|
| Reporting group title | Usual care |
|-----------------------|------------|

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The trial tests a therapeutic strategy evaluating approved therapies in their approved indication. Therefore, the collection of adverse events was limited to SUSARs and to events related to the intervention. Details have been published in the trial protocol (refer to NEJM online appendix).

| Serious adverse events  | Early rhythm control                                | Usual care             |  |
|---|---|------------------------|--|
| Total subjects affected by serious adverse events                   |   |                        |  |
| subjects affected / exposed   | 978 / 1395<br>(70.11%)                              | 999 / 1394<br>(71.66%) |  |
| number of deaths (all causes)                                       | 138   | 165                    |  |
| number of deaths resulting from adverse events                      | 138   | 165                    |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                        |  |
| Abdominal neoplasm  | Additional description: Abdominal neoplasm          |                        |  |
| subjects affected / exposed   | 1 / 1395 (0.07%)                                    | 2 / 1394 (0.14%)       |  |
| occurrences causally related to treatment / all                     | 0 / 1   | 0 / 2                  |  |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0                  |  |
| Acute lymphocytic leukaemia   | Additional description: Acute lymphocytic leukaemia |                        |  |
| subjects affected / exposed   | 2 / 1395 (0.14%)                                    | 0 / 1394 (0.00%)       |  |
| occurrences causally related to treatment / all                     | 0 / 2   | 0 / 0                  |  |
| deaths causally related to treatment / all                          | 0 / 1   | 0 / 0                  |  |
| Acute myeloid leukaemia   | Additional description: Acute myeloid leukaemia     |                        |  |
| subjects affected / exposed   | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%)       |  |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 1                  |  |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0                  |  |
| Adenocarcinoma gastric  | Additional description: Adenocarcinoma gastric      |                        |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1             |  |
| Adenoma benign                                  | Additional description: Adenoma benign                           |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Adrenal adenoma                                 | Additional description: Adrenal adenoma                          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Anal cancer                                     | Additional description: Anal cancer                              |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1             |  |
| Angiosarcoma                                    | Additional description: Angiosarcoma                             |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0             |  |
| Basal cell carcinoma                            | Additional description: Basal cell carcinoma                     |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)   | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Basosquamous carcinoma of skin                  | Additional description: Basosquamous carcinoma of skin           |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Bladder adenocarcinoma stage unspecified        | Additional description: Bladder adenocarcinoma stage unspecified |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)   | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0             |  |
| Bladder cancer                                  | Additional description: Bladder cancer                           |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 8 / 1395 (0.57%)  | 7 / 1394 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 10  | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Brain neoplasm                                  | Additional description: Brain neoplasm                  |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Breast cancer                                   | Additional description: Breast cancer                   |                   |  |
| subjects affected / exposed                     | 10 / 1395 (0.72%)                                       | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 12  | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0             |  |
| Bronchial carcinoma                             | Additional description: Bronchial carcinoma             |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0             |  |
| Carcinoid tumour                                | Additional description: Carcinoid tumour                |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Carcinoma in situ                               | Additional description: Carcinoma in situ               |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardiac myxoma                                  | Additional description: Cardiac myxoma                  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Central nervous system lymphoma                 | Additional description: Central nervous system lymphoma |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Cervix carcinoma                                | Additional description: Cervix carcinoma                |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Chronic myeloid leukaemia                       | Additional description: Chronic myeloid leukaemia     |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Colon cancer                                    | Additional description: Colon cancer                  |                   |  |
| subjects affected / exposed                     | 10 / 1395 (0.72%)                                     | 17 / 1394 (1.22%) |  |
| occurrences causally related to treatment / all | 0 / 13  | 0 / 19            |  |
| deaths causally related to treatment / all      | 0 / 4   | 0 / 0             |  |
| Colorectal cancer                               | Additional description: Colorectal cancer             |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 5   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 2   | 0 / 0             |  |
| Endometrial cancer                              | Additional description: Endometrial cancer            |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0             |  |
| Gallbladder cancer                              | Additional description: Gallbladder cancer            |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Gallbladder cancer metastatic                   | Additional description: Gallbladder cancer metastatic |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Gastric cancer                                  | Additional description: Gastric cancer                |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Gastrointestinal neoplasm                       | Additional description: Gastrointestinal neoplasm     |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Glioblastoma                                    |   |                  |  |
|   | Additional description: Glioblastoma                  |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 1            |  |
| Hairy cell leukaemia                            |   |                  |  |
|   | Additional description: Hairy cell leukaemia          |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hepatic cancer                                  |   |                  |  |
|   | Additional description: Hepatic cancer                |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hepatocellular carcinoma                        |   |                  |  |
|   | Additional description: Hepatocellular carcinoma      |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0            |  |
| Intestinal adenocarcinoma                       |   |                  |  |
|   | Additional description: Intestinal adenocarcinoma     |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Laryngeal cancer                                |   |                  |  |
|   | Additional description: Laryngeal cancer              |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Leukaemia                                       |   |                  |  |
|   | Additional description: Leukaemia                     |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Lip and/or oral cavity cancer                   |   |                  |  |
|   | Additional description: Lip and/or oral cavity cancer |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Lung adenocarcinoma                             | Additional description: Lung adenocarcinoma          |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Lung cancer metastatic                          | Additional description: Lung cancer metastatic       |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Lung neoplasm                                   | Additional description: Lung neoplasm                |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Lung neoplasm malignant                         | Additional description: Lung neoplasm malignant      |                   |  |
| subjects affected / exposed                     | 10 / 1395 (0.72%)                                    | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 24   | 0 / 22            |  |
| deaths causally related to treatment / all      | 0 / 4  | 0 / 7             |  |
| Lymphoma  | Additional description: Lymphoma                     |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                     | 8 / 1394 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 14   | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 2  | 0 / 1             |  |
| Malignant ascites                               | Additional description: Malignant ascites            |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Malignant melanoma                              | Additional description: Malignant melanoma           |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                     | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1             |  |
| Malignant neoplasm of thymus                    | Additional description: Malignant neoplasm of thymus |                   |  |



|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1            |  |
| Malignant neoplasm of uterine adnexa            | Additional description: Malignant neoplasm of uterine adnexa |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Mediastinum neoplasm                            | Additional description: Mediastinum neoplasm                 |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1            |  |
| Meningioma benign                               | Additional description: Meningioma benign                    |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Mesothelioma                                    | Additional description: Mesothelioma                         |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Metastases to lung                              | Additional description: Metastases to lung                   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Metastasis                                      | Additional description: Metastasis                           |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0            |  |
| Metastatic neoplasm                             | Additional description: Metastatic neoplasm                  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Myelodysplastic syndrome                        | Additional description: Myelodysplastic syndrome             |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Neoplasm  | Additional description: Neoplasm                             |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1            |  |
| Neoplasm malignant                              | Additional description: Neoplasm malignant                   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 3            |  |
| Neoplasm skin                                   | Additional description: Neoplasm skin                        |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Neuroendocrine carcinoma of the skin            | Additional description: Neuroendocrine carcinoma of the skin |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Neurofibrosarcoma                               | Additional description: Neurofibrosarcoma                    |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Oesophageal carcinoma                           | Additional description: Oesophageal carcinoma                |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Ovarian cancer                                  | Additional description: Ovarian cancer                       |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 2  | 0 / 0            |  |
| Pancreatic carcinoma                            | Additional description: Pancreatic carcinoma                 |                  |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 9 / 1395 (0.65%)  | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 14  | 0 / 43            |  |
| deaths causally related to treatment / all      | 0 / 5   | 0 / 6             |  |
| Pancreatic carcinoma metastatic                 | Additional description: Pancreatic carcinoma metastatic |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Penile cancer                                   | Additional description: Penile cancer                   |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Plasma cell myeloma                             | Additional description: Plasma cell myeloma             |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Prostate cancer                                 | Additional description: Prostate cancer                 |                   |  |
| subjects affected / exposed                     | 18 / 1395 (1.29%)                                       | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 24  | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 4   | 0 / 2             |  |
| Prostate cancer metastatic                      | Additional description: Prostate cancer metastatic      |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Prostatic adenoma                               | Additional description: Prostatic adenoma               |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Rectal adenocarcinoma                           | Additional description: Rectal adenocarcinoma           |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Rectal cancer                                   | Additional description: Rectal cancer                   |                   |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 6 / 1395 (0.43%)   | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 7  | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Renal cancer                                    | Additional description: Renal cancer                       |                  |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)   | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1            |  |
| Salivary gland neoplasm                         | Additional description: Salivary gland neoplasm            |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Skin cancer                                     | Additional description: Skin cancer                        |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Skin cancer metastatic                          | Additional description: Skin cancer metastatic             |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Small intestine carcinoma                       | Additional description: Small intestine carcinoma          |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Soft tissue neoplasm                            | Additional description: Soft tissue neoplasm               |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Squamous cell carcinoma of pharynx              | Additional description: Squamous cell carcinoma of pharynx |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Thyroid adenoma                                 | Additional description: Thyroid adenoma                    |                  |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Thyroid cancer                                  | Additional description: Thyroid cancer              |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Tonsil cancer                                   | Additional description: Tonsil cancer               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Transitional cell carcinoma                     | Additional description: Transitional cell carcinoma |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                    | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1            |  |
| Urethral cancer                                 | Additional description: Urethral cancer             |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                    | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Uterine cancer                                  | Additional description: Uterine cancer              |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Vulval cancer                                   | Additional description: Vulval cancer               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Vascular disorders                              |   |                  |  |
| Aortic aneurysm                                 | Additional description: Aortic aneurysm             |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0            |  |
| Aortic dissection                               | Additional description: Aortic dissection           |                  |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)                              | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 2             |  |
| Aortic stenosis                                 | Additional description: Aortic stenosis       |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                              | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Arteriovenous fistula                           | Additional description: Arteriovenous fistula |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Circulatory collapse                            | Additional description: Circulatory collapse  |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                              | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Deep vein thrombosis                            | Additional description: Deep vein thrombosis  |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                              | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Embolism arterial                               | Additional description: Embolism arterial     |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Haematoma                                       | Additional description: Haematoma             |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                              | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Haemorrhage                                     | Additional description: Haemorrhage           |                   |  |
| subjects affected / exposed                     | 73 / 1395 (5.23%)                             | 83 / 1394 (5.95%) |  |
| occurrences causally related to treatment / all | 1 / 81  | 1 / 97            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 10            |  |
| Hypertension                                    | Additional description: Hypertension          |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 34 / 1395 (2.44%)   | 41 / 1394 (2.94%) |  |
| occurrences causally related to treatment / all | 1 / 36  | 0 / 49            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hypertensive crisis                             | Additional description: Hypertensive crisis                   |                   |  |
| subjects affected / exposed                     | 11 / 1395 (0.79%)   | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 11  | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hypotension                                     | Additional description: Hypotension                           |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Iliac artery stenosis                           | Additional description: Iliac artery stenosis                 |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Peripheral arterial occlusive disease           | Additional description: Peripheral arterial occlusive disease |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 6 / 1394 (0.43%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Peripheral embolism                             | Additional description: Peripheral embolism                   |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Peripheral ischaemia                            | Additional description: Peripheral ischaemia                  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Post thrombotic syndrome                        | Additional description: Post thrombotic syndrome              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Renovascular hypertension                       | Additional description: Renovascular hypertension             |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Temporal arteritis                              | Additional description: Temporal arteritis                            |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Thrombophlebitis                                | Additional description: Thrombophlebitis                              |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Vasculitis                                      | Additional description: Vasculitis                                    |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Surgical and medical procedures                 |   |                  |  |
| Abdominal operation                             | Additional description: Abdominal operation                           |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)  | 7 / 1394 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 5   | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Adrenalectomy                                   | Additional description: Adrenalectomy                                 |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Alcohol detoxification                          | Additional description: Alcohol detoxification                        |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Alcohol rehabilitation                          | Additional description: Alcohol rehabilitation                        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Allogenic bone marrow transplantation therapy   | Additional description: Allogenic bone marrow transplantation therapy |                  |  |



|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Angioplasty                                     | Additional description: Angioplasty                     |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Ankle operation                                 | Additional description: Ankle operation                 |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 5   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Anorectal operation                             | Additional description: Anorectal operation             |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Aortic aneurysm repair                          | Additional description: Aortic aneurysm repair          |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Aortic valve replacement                        | Additional description: Aortic valve replacement        |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Appendicectomy                                  | Additional description: Appendicectomy                  |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Arterial repair                                 | Additional description: Arterial repair                 |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Arteriovenous fistula operation                 | Additional description: Arteriovenous fistula operation |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Arthrodesis                                     | Additional description: Arthrodesis                          |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Arthroscopic surgery                            | Additional description: Arthroscopic surgery                 |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Artificial urinary sphincter implant            | Additional description: Artificial urinary sphincter implant |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Atherectomy                                     | Additional description: Atherectomy                          |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Atrial septal defect repair                     | Additional description: Atrial septal defect repair          |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Baker's cyst excision                           | Additional description: Baker's cyst excision                |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Bile duct stent removal                         | Additional description: Bile duct stent removal              |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Bladder neoplasm surgery                        | Additional description: Bladder neoplasm surgery             |                  |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Bladder operation                               | Additional description: Bladder operation                 |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Caesarean section                               | Additional description: Caesarean section                 |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardiac ablation                                | Additional description: Cardiac ablation                  |                   |  |
| subjects affected / exposed                     | 27 / 1395 (1.94%)   | 20 / 1394 (1.43%) |  |
| occurrences causally related to treatment / all | 4 / 27  | 1 / 21            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardiac operation                               | Additional description: Cardiac operation                 |                   |  |
| subjects affected / exposed                     | 15 / 1395 (1.08%)   | 14 / 1394 (1.00%) |  |
| occurrences causally related to treatment / all | 0 / 15  | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardiac pacemaker insertion                     | Additional description: Cardiac pacemaker insertion       |                   |  |
| subjects affected / exposed                     | 88 / 1395 (6.31%)   | 83 / 1394 (5.95%) |  |
| occurrences causally related to treatment / all | 11 / 90   | 4 / 88            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Cardiac pacemaker replacement                   | Additional description: Cardiac pacemaker replacement     |                   |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 7   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardiac resynchronisation therapy               | Additional description: Cardiac resynchronisation therapy |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardioversion                                   | Additional description: Cardioversion                     |                   |  |

|   |  |                        |  |
|---|--|------------------------|--|
| subjects affected / exposed                     | 225 / 1395<br>(16.13%)                                 | 223 / 1394<br>(16.00%) |  |
| occurrences causally related to treatment / all | 4 / 357  | 5 / 390                |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Carotid endarterectomy                          | Additional description: Carotid endarterectomy         |                        |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)                                       | 1 / 1394 (0.07%)       |  |
| occurrences causally related to treatment / all | 0 / 7  | 0 / 1                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Cataract operation                              | Additional description: Cataract operation             |                        |  |
| subjects affected / exposed                     | 11 / 1395 (0.79%)                                      | 4 / 1394 (0.29%)       |  |
| occurrences causally related to treatment / all | 0 / 15   | 0 / 5                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Central venous catheterisation                  | Additional description: Central venous catheterisation |                        |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%)       |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Cervical polypectomy                            | Additional description: Cervical polypectomy           |                        |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%)       |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Chemotherapy                                    | Additional description: Chemotherapy                   |                        |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                       | 2 / 1394 (0.14%)       |  |
| occurrences causally related to treatment / all | 0 / 12   | 0 / 2                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Cholecystectomy                                 | Additional description: Cholecystectomy                |                        |  |
| subjects affected / exposed                     | 16 / 1395 (1.15%)                                      | 17 / 1394 (1.22%)      |  |
| occurrences causally related to treatment / all | 0 / 17   | 0 / 17                 |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Circumcision                                    | Additional description: Circumcision                   |                        |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%)       |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Colectomy                                       | Additional description: Colectomy                      |                        |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Colon operation                                 | Additional description: Colon operation        |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                               | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Colostomy                                       | Additional description: Colostomy              |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                               | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Coronary angioplasty                            | Additional description: Coronary angioplasty   |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Coronary artery bypass                          | Additional description: Coronary artery bypass |                   |  |
| subjects affected / exposed                     | 14 / 1395 (1.00%)                              | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 14   | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Cox-Maze procedure                              | Additional description: Cox-Maze procedure     |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Dacryocystorhinostomy                           | Additional description: Dacryocystorhinostomy  |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Debridement                                     | Additional description: Debridement            |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Elbow operation                                 | Additional description: Elbow operation        |                   |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Endarterectomy                                  | Additional description: Endarterectomy           |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Enterostomy                                     | Additional description: Enterostomy              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Eye operation                                   | Additional description: Eye operation            |                   |  |
| subjects affected / exposed                     | 8 / 1395 (0.57%)                                 | 12 / 1394 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 8  | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Eyelid operation                                | Additional description: Eyelid operation         |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Foot operation                                  | Additional description: Foot operation           |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Foraminotomy                                    | Additional description: Foraminotomy             |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Gastric operation                               | Additional description: Gastric operation        |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Gastrointestinal surgery                        | Additional description: Gastrointestinal surgery |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Gastrostomy                                     | Additional description: Gastrostomy             |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Glaucoma surgery                                | Additional description: Glaucoma surgery        |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Haemorrhoid operation                           | Additional description: Haemorrhoid operation   |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Heart valve operation                           | Additional description: Heart valve operation   |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Heart valve replacement                         | Additional description: Heart valve replacement |                   |  |
| subjects affected / exposed                     | 11 / 1395 (0.79%)                               | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 11  | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hernia repair                                   | Additional description: Hernia repair           |                   |  |
| subjects affected / exposed                     | 13 / 1395 (0.93%)                               | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 13  | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hip arthroplasty                                | Additional description: Hip arthroplasty        |                   |  |
| subjects affected / exposed                     | 42 / 1395 (3.01%)                               | 43 / 1394 (3.08%) |  |
| occurrences causally related to treatment / all | 0 / 48  | 0 / 47            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hip surgery                                     | Additional description: Hip surgery             |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 9 / 1395 (0.65%)  | 12 / 1394 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 11  | 0 / 18            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hydrocele operation                             | Additional description: Hydrocele operation                   |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hysterectomy                                    | Additional description: Hysterectomy                          |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Ileostomy                                       | Additional description: Ileostomy                             |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Implantable defibrillator insertion             | Additional description: Implantable defibrillator insertion   |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Implantable defibrillator replacement           | Additional description: Implantable defibrillator replacement |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Inguinal hernia repair                          | Additional description: Inguinal hernia repair                |                   |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)  | 6 / 1394 (0.43%)  |  |
| occurrences causally related to treatment / all | 0 / 8   | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Intervertebral disc operation                   | Additional description: Intervertebral disc operation         |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Intestinal operation                            | Additional description: Intestinal operation                  |                   |  |



|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Intra-cerebral aneurysm operation               | Additional description: Intra-cerebral aneurysm operation |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Joint arthroplasty                              | Additional description: Joint arthroplasty                |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Joint resurfacing surgery                       | Additional description: Joint resurfacing surgery         |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Keratomileusis                                  | Additional description: Keratomileusis                    |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Knee arthroplasty                               | Additional description: Knee arthroplasty                 |                   |  |
| subjects affected / exposed                     | 36 / 1395 (2.58%)   | 39 / 1394 (2.80%) |  |
| occurrences causally related to treatment / all | 0 / 39  | 0 / 46            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Knee operation                                  | Additional description: Knee operation                    |                   |  |
| subjects affected / exposed                     | 19 / 1395 (1.36%)   | 26 / 1394 (1.87%) |  |
| occurrences causally related to treatment / all | 0 / 19  | 0 / 27            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Laparotomy                                      | Additional description: Laparotomy                        |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Large intestinal polypectomy                    | Additional description: Large intestinal polypectomy      |                   |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Laryngeal operation                             | Additional description: Laryngeal operation    |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Limb operation                                  | Additional description: Limb operation         |                  |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)                               | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Lithotripsy                                     | Additional description: Lithotripsy            |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Lung neoplasm surgery                           | Additional description: Lung neoplasm surgery  |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Lymphadenectomy                                 | Additional description: Lymphadenectomy        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Mammoplasty                                     | Additional description: Mammoplasty            |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Mastectomy                                      | Additional description: Mastectomy             |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Medical device removal                          | Additional description: Medical device removal |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Meningioma surgery                              | Additional description: Meningioma surgery       |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Meniscus operation                              | Additional description: Meniscus operation       |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Meniscus removal                                | Additional description: Meniscus removal         |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Metabolic surgery                               | Additional description: Metabolic surgery        |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                 | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Mitral valve repair                             | Additional description: Mitral valve repair      |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                 | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 5  | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Mitral valve replacement                        | Additional description: Mitral valve replacement |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Nasal operation                                 | Additional description: Nasal operation          |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Nephrectomy                                     | Additional description: Nephrectomy              |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Orthopaedic procedure                           | Additional description: Orthopaedic procedure              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Otorhinolaryngological surgery                  | Additional description: Otorhinolaryngological surgery     |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Pancreatectomy                                  | Additional description: Pancreatectomy                     |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Parathyroidectomy                               | Additional description: Parathyroidectomy                  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Parotidectomy                                   | Additional description: Parotidectomy                      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Pelvic floor repair                             | Additional description: Pelvic floor repair                |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Percutaneous coronary intervention              | Additional description: Percutaneous coronary intervention |                   |  |
| subjects affected / exposed                     | 65 / 1395 (4.66%)  | 57 / 1394 (4.09%) |  |
| occurrences causally related to treatment / all | 0 / 77   | 0 / 69            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Peripheral artery angioplasty                   | Additional description: Peripheral artery angioplasty      |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 18 / 1395 (1.29%)                                 | 23 / 1394 (1.65%) |  |
| occurrences causally related to treatment / all | 0 / 27  | 0 / 31            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Peripheral artery bypass                        | Additional description: Peripheral artery bypass  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Peripheral endarterectomy                       | Additional description: Peripheral endarterectomy |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Phlebectomy                                     | Additional description: Phlebectomy               |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Pituitary tumour removal                        | Additional description: Pituitary tumour removal  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Plastic surgery                                 | Additional description: Plastic surgery           |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Pleurectomy                                     | Additional description: Pleurectomy               |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Polypectomy                                     | Additional description: Polypectomy               |                   |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 8   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Prostatectomy                                   | Additional description: Prostatectomy             |                   |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                   | 14 / 1394 (1.00%) |  |
| occurrences causally related to treatment / all | 0 / 5  | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Prostatic operation                             | Additional description: Prostatic operation        |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Radioactive iodine therapy                      | Additional description: Radioactive iodine therapy |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 5  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Radiotherapy                                    | Additional description: Radiotherapy               |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Rectal prolapse repair                          | Additional description: Rectal prolapse repair     |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Renal stone removal                             | Additional description: Renal stone removal        |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Renal surgery                                   | Additional description: Renal surgery              |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                   | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Resuscitation                                   | Additional description: Resuscitation              |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Rhinoplasty                                     | Additional description: Rhinoplasty                |                   |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Salivary gland operation                        | Additional description: Salivary gland operation |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Salpingo-oophorectomy                           | Additional description: Salpingo-oophorectomy    |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Shoulder arthroplasty                           | Additional description: Shoulder arthroplasty    |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Shoulder operation                              | Additional description: Shoulder operation       |                   |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)                                 | 12 / 1394 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 7  | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Sinus operation                                 | Additional description: Sinus operation          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Skin cosmetic procedure                         | Additional description: Skin cosmetic procedure  |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Skin graft                                      | Additional description: Skin graft               |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Skin neoplasm excision                          | Additional description: Skin neoplasm excision   |                   |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                 | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Skin operation                                  | Additional description: Skin operation           |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Spinal laminectomy                              | Additional description: Spinal laminectomy       |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Spinal operation                                | Additional description: Spinal operation         |                   |  |
| subjects affected / exposed                     | 18 / 1395 (1.29%)                                | 23 / 1394 (1.65%) |  |
| occurrences causally related to treatment / all | 0 / 19   | 0 / 27            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Surgery   | Additional description: Surgery                  |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                 | 6 / 1394 (0.43%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Tendon operation                                | Additional description: Tendon operation         |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Therapeutic embolisation                        | Additional description: Therapeutic embolisation |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Thrombectomy                                    | Additional description: Thrombectomy             |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Thromboembolectomy                              | Additional description: Thromboembolectomy       |                   |  |



|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Thyroidectomy                                   | Additional description: Thyroidectomy                   |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Toe amputation                                  | Additional description: Toe amputation                  |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Toe operation                                   | Additional description: Toe operation                   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Tonsillectomy                                   | Additional description: Tonsillectomy                   |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Tooth extraction                                | Additional description: Tooth extraction                |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Tracheostomy tube removal                       | Additional description: Tracheostomy tube removal       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Transurethral bladder resection                 | Additional description: Transurethral bladder resection |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Transurethral prostatectomy                     | Additional description: Transurethral prostatectomy     |                  |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Tricuspid valve repair                          | Additional description: Tricuspid valve repair    |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Tympanoplasty                                   | Additional description: Tympanoplasty             |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Umbilical hernia repair                         | Additional description: Umbilical hernia repair   |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Urethral caruncle removal                       | Additional description: Urethral caruncle removal |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Urethral operation                              | Additional description: Urethral operation        |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Urethrotomy                                     | Additional description: Urethrotomy               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Urinary tract operation                         | Additional description: Urinary tract operation   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Uterine operation                               | Additional description: Uterine operation         |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Vaginal operation                               | Additional description: Vaginal operation                |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Varicose vein operation                         | Additional description: Varicose vein operation          |                  |  |
| subjects affected / exposed                     | 11 / 1395 (0.79%)  | 9 / 1394 (0.65%) |  |
| occurrences causally related to treatment / all | 0 / 12   | 0 / 12           |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Ventricular septal defect repair                | Additional description: Ventricular septal defect repair |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Vertebroplasty                                  | Additional description: Vertebroplasty                   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Vitrectomy                                      | Additional description: Vitrectomy                       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Vocal cord nodule removal                       | Additional description: Vocal cord nodule removal        |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Wound treatment                                 | Additional description: Wound treatment                  |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Wrist surgery                                   | Additional description: Wrist surgery                    |                  |  |

|  |   |                    |  |
|--|---|--------------------|--|
| subjects affected / exposed                          | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%)   |  |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 1              |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0              |  |
| General disorders and administration site conditions |   |                    |  |
| Asthenia   | Additional description: Asthenia                  |                    |  |
| subjects affected / exposed                          | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%)   |  |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 1              |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0              |  |
| Cardiac death  | Additional description: Cardiac death             |                    |  |
| subjects affected / exposed                          | 19 / 1395 (1.36%)                                 | 22 / 1394 (1.58%)  |  |
| occurrences causally related to treatment / all      | 0 / 19  | 0 / 22             |  |
| deaths causally related to treatment / all           | 0 / 19  | 0 / 21             |  |
| Catheter site haemorrhage                            | Additional description: Catheter site haemorrhage |                    |  |
| subjects affected / exposed                          | 8 / 1395 (0.57%)                                  | 4 / 1394 (0.29%)   |  |
| occurrences causally related to treatment / all      | 5 / 8   | 1 / 4              |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0              |  |
| Chest pain   | Additional description: Chest pain                |                    |  |
| subjects affected / exposed                          | 25 / 1395 (1.79%)                                 | 12 / 1394 (0.86%)  |  |
| occurrences causally related to treatment / all      | 0 / 28  | 0 / 13             |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0              |  |
| Death  | Additional description: Death                     |                    |  |
| subjects affected / exposed                          | 109 / 1395 (7.81%)                                | 131 / 1394 (9.40%) |  |
| occurrences causally related to treatment / all      | 0 / 109   | 1 / 131            |  |
| deaths causally related to treatment / all           | 0 / 109   | 1 / 131            |  |
| Discomfort   | Additional description: Discomfort                |                    |  |
| subjects affected / exposed                          | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%)   |  |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 1              |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0              |  |
| Extravasation  | Additional description: Extravasation             |                    |  |
| subjects affected / exposed                          | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%)   |  |
| occurrences causally related to treatment / all      | 0 / 0   | 0 / 1              |  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0              |  |
| Gait disturbance                                     | Additional description: Gait disturbance          |                    |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| General physical health deterioration           | Additional description: General physical health deterioration |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hernia  | Additional description: Hernia                                |                  |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)  | 7 / 1394 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 7   | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hypothermia                                     | Additional description: Hypothermia                           |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 1            |  |
| Impaired healing                                | Additional description: Impaired healing                      |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Multiple organ dysfunction syndrome             | Additional description: Multiple organ dysfunction syndrome   |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 2            |  |
| Necrosis  | Additional description: Necrosis                              |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Oedema  | Additional description: Oedema                                |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Oedema peripheral                               | Additional description: Oedema peripheral                     |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                       | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0             |  |
| Pacemaker generated arrhythmia                  | Additional description: Pacemaker generated arrhythmia |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Pain  | Additional description: Pain                           |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Pyrexia   | Additional description: Pyrexia                        |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Stent-graft endoleak                            | Additional description: Stent-graft endoleak           |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Strangulated hernia                             | Additional description: Strangulated hernia            |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Sudden cardiac death                            | Additional description: Sudden cardiac death           |                   |  |
| subjects affected / exposed                     | 8 / 1395 (0.57%)                                       | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 8  | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 8  | 0 / 11            |  |
| Sudden death                                    | Additional description: Sudden death                   |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                       | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 2  | 0 / 2             |  |
| Vascular stent thrombosis                       | Additional description: Vascular stent thrombosis      |                   |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1            |  |
| Immune system disorders                         |  |                  |  |
| Amyloidosis                                     | Additional description: Amyloidosis                  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Drug hypersensitivity                           | Additional description: Drug hypersensitivity        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hypersensitivity                                | Additional description: Hypersensitivity             |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                     | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Reproductive system and breast disorders        |  |                  |  |
| Benign prostatic hyperplasia                    | Additional description: Benign prostatic hyperplasia |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                     | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Female genital tract fistula                    | Additional description: Female genital tract fistula |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pelvic pain                                     | Additional description: Pelvic pain                  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Prostatitis                                     | Additional description: Prostatitis                  |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |

|   |   |                   |  |
|---|---|-------------------|--|
| Respiratory, thoracic and mediastinal disorders |   |                   |  |
| Acute respiratory failure                       | Additional description: Acute respiratory failure             |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Asthma  | Additional description: Asthma                                |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)  | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 9   | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Atelectasis                                     | Additional description: Atelectasis                           |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Bronchopulmonary disease                        | Additional description: Bronchopulmonary disease              |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Chronic obstructive pulmonary disease           | Additional description: Chronic obstructive pulmonary disease |                   |  |
| subjects affected / exposed                     | 24 / 1395 (1.72%)   | 28 / 1394 (2.01%) |  |
| occurrences causally related to treatment / all | 0 / 41  | 0 / 41            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 2             |  |
| Dyspnoea  | Additional description: Dyspnoea                              |                   |  |
| subjects affected / exposed                     | 15 / 1395 (1.08%)   | 12 / 1394 (0.86%) |  |
| occurrences causally related to treatment / all | 1 / 15  | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Dyspnoea exertional                             | Additional description: Dyspnoea exertional                   |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Epistaxis                                       | Additional description: Epistaxis                             |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)  | 9 / 1394 (0.65%)  |  |
| occurrences causally related to treatment / all | 0 / 5   | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |



|   |   |                  |  |
|---|---|------------------|--|
| Haemoptysis                                     | Additional description: Haemoptysis               |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 1 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Haemothorax                                     | Additional description: Haemothorax               |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hiccups   | Additional description: Hiccups                   |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hyperventilation                                | Additional description: Hyperventilation          |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Interstitial lung disease                       | Additional description: Interstitial lung disease |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Lung infiltration                               | Additional description: Lung infiltration         |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Pleural effusion                                | Additional description: Pleural effusion          |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Pneumonia aspiration                            | Additional description: Pneumonia aspiration      |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1            |  |
| Pneumothorax                                    | Additional description: Pneumothorax              |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pulmonary embolism                              | Additional description: Pulmonary embolism     |                  |  |
| subjects affected / exposed                     | 11 / 1395 (0.79%)                              | 8 / 1394 (0.57%) |  |
| occurrences causally related to treatment / all | 0 / 13   | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 4  | 0 / 2            |  |
| Pulmonary fibrosis                              | Additional description: Pulmonary fibrosis     |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                               | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 1 / 2  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1            |  |
| Pulmonary hypertension                          | Additional description: Pulmonary hypertension |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                               | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 7  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pulmonary oedema                                | Additional description: Pulmonary oedema       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pulmonary sarcoidosis                           | Additional description: Pulmonary sarcoidosis  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Respiratory failure                             | Additional description: Respiratory failure    |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                               | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0            |  |
| Sleep apnoea syndrome                           | Additional description: Sleep apnoea syndrome  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Vocal cord disorder                             | Additional description: Vocal cord disorder    |                  |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Psychiatric disorders                           |   |                  |  |
| Alcohol withdrawal syndrome                     | Additional description: Alcohol withdrawal syndrome |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Alcoholism                                      | Additional description: Alcoholism                  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Anxiety disorder                                | Additional description: Anxiety disorder            |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Completed suicide                               | Additional description: Completed suicide           |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1            |  |
| Delirium  | Additional description: Delirium                    |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                    | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Depression                                      | Additional description: Depression                  |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                    | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Panic attack                                    | Additional description: Panic attack                |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Product issues                                  |   |                  |  |

|   |   |                  |  |
|---|---|------------------|--|
| Device lead issue                               | Additional description: Device lead issue         |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Device occlusion                                | Additional description: Device occlusion          |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Device power source issue                       | Additional description: Device power source issue |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Lead dislodgement                               | Additional description: Lead dislodgement         |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hepatobiliary disorders                         |   |                  |  |
| Acute hepatic failure                           | Additional description: Acute hepatic failure     |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0            |  |
| Autoimmune hepatitis                            | Additional description: Autoimmune hepatitis      |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Bile duct stone                                 | Additional description: Bile duct stone           |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cholangitis                                     | Additional description: Cholangitis               |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cholecystitis                                   | Additional description: Cholecystitis             |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 7 / 1395 (0.50%)                               | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 7  | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Cholecystitis acute                             | Additional description: Cholecystitis acute    |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Cholelithiasis                                  | Additional description: Cholelithiasis         |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                               | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hepatic cirrhosis                               | Additional description: Hepatic cirrhosis      |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hepatic cyst                                    | Additional description: Hepatic cyst           |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hepatitis                                       | Additional description: Hepatitis              |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hepatitis toxic                                 | Additional description: Hepatitis toxic        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 1 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Portal vein thrombosis                          | Additional description: Portal vein thrombosis |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Investigations                                  |  |                  |  |
| Angiogram                                       | Additional description: Angiogram              |                  |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 31 / 1395 (2.22%)   | 16 / 1394 (1.15%) |  |
| occurrences causally related to treatment / all | 0 / 32  | 0 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Arthroscopy                                     | Additional description: Arthroscopy                                 |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Biopsy bone                                     | Additional description: Biopsy bone                                 |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Biopsy breast                                   | Additional description: Biopsy breast                               |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Biopsy lung normal                              | Additional description: Biopsy lung normal                          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Biopsy lymph gland                              | Additional description: Biopsy lymph gland                          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Biopsy prostate                                 | Additional description: Biopsy prostate                             |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Blood thyroid stimulating hormone increased     | Additional description: Blood thyroid stimulating hormone increased |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Bronchoscopy                                    | Additional description: Bronchoscopy                                |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| C-reactive protein increased                    | Additional description: C-reactive protein increased      |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cardiac monitoring                              | Additional description: Cardiac monitoring                |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cardiac pacemaker evaluation                    | Additional description: Cardiac pacemaker evaluation      |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cardiac pharmacologic stress test               | Additional description: Cardiac pharmacologic stress test |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cardiac stress test                             | Additional description: Cardiac stress test               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cardiovascular evaluation                       | Additional description: Cardiovascular evaluation         |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Colonoscopy                                     | Additional description: Colonoscopy                       |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Diagnostic procedure                            | Additional description: Diagnostic procedure              |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Echocardiogram                                  | Additional description: Echocardiogram                 |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Electrocardiogram QT prolonged                  | Additional description: Electrocardiogram QT prolonged |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Gynaecological examination                      | Additional description: Gynaecological examination     |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Haemoglobin decreased                           | Additional description: Haemoglobin decreased          |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hepatic enzyme increased                        | Additional description: Hepatic enzyme increased       |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hysteroscopy                                    | Additional description: Hysteroscopy                   |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Magnetic resonance imaging                      | Additional description: Magnetic resonance imaging     |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Stress echocardiogram                           | Additional description: Stress echocardiogram          |                  |  |



|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Troponin increased                              | Additional description: Troponin increased      |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Tumour marker increased                         | Additional description: Tumour marker increased |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Viral test negative                             | Additional description: Viral test negative     |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Weight decreased                                | Additional description: Weight decreased        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Injury, poisoning and procedural complications  |   |                  |  |
| Alcohol poisoning                               | Additional description: Alcohol poisoning       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Anaemia postoperative                           | Additional description: Anaemia postoperative   |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Animal bite                                     | Additional description: Animal bite             |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Ankle fracture                                  | Additional description: Ankle fracture          |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 6 / 1395 (0.43%)   | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Arthropod bite                                  | Additional description: Arthropod bite                       |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Buttock injury                                  | Additional description: Buttock injury                       |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Cervical vertebral fracture                     | Additional description: Cervical vertebral fracture          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Clavicle fracture                               | Additional description: Clavicle fracture                    |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Craniocerebral injury                           | Additional description: Craniocerebral injury                |                   |  |
| subjects affected / exposed                     | 9 / 1395 (0.65%)   | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 10   | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 1             |  |
| Endotracheal intubation complication            | Additional description: Endotracheal intubation complication |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Facial bones fracture                           | Additional description: Facial bones fracture                |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)   | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 5  | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Fall  | Additional description: Fall                                 |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 14 / 1395 (1.00%)   | 10 / 1394 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 14  | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Femur fracture                                  | Additional description: Femur fracture                      |                   |  |
| subjects affected / exposed                     | 11 / 1395 (0.79%)   | 8 / 1394 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 14  | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 2             |  |
| Fibula fracture                                 | Additional description: Fibula fracture                     |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Foot fracture                                   | Additional description: Foot fracture                       |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Fractured sacrum                                | Additional description: Fractured sacrum                    |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Gastrointestinal stoma complication             | Additional description: Gastrointestinal stoma complication |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hand fracture                                   | Additional description: Hand fracture                       |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Head injury                                     | Additional description: Head injury                         |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hip fracture                                    | Additional description: Hip fracture                        |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 12 / 1394 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Humerus fracture                                | Additional description: Humerus fracture          |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                  | 15 / 1394 (1.08%) |  |
| occurrences causally related to treatment / all | 0 / 5   | 1 / 16            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Injury  | Additional description: Injury                    |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 7 / 1394 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Joint dislocation                               | Additional description: Joint dislocation         |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                  | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 9   | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Laryngeal injury                                | Additional description: Laryngeal injury          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Limb crushing injury                            | Additional description: Limb crushing injury      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Limb injury                                     | Additional description: Limb injury               |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Lower limb fracture                             | Additional description: Lower limb fracture       |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Lumbar vertebral fracture                       | Additional description: Lumbar vertebral fracture |                   |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Multiple injuries                               | Additional description: Multiple injuries            |                  |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)                                     | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 7  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 1            |  |
| Nerve injury                                    | Additional description: Nerve injury                 |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Overdose  | Additional description: Overdose                     |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                     | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Patella fracture                                | Additional description: Patella fracture             |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pelvic fracture                                 | Additional description: Pelvic fracture              |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                     | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 5  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Post-traumatic neck syndrome                    | Additional description: Post-traumatic neck syndrome |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Post procedural complication                    | Additional description: Post procedural complication |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Post procedural haematoma                       | Additional description: Post procedural haematoma    |                  |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Post procedural haemorrhage                     | Additional description: Post procedural haemorrhage                   |                   |  |
| subjects affected / exposed                     | 26 / 1395 (1.86%)   | 26 / 1394 (1.87%) |  |
| occurrences causally related to treatment / all | 1 / 26  | 0 / 26            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Postoperative thoracic procedure complication   | Additional description: Postoperative thoracic procedure complication |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Procedural intestinal perforation               | Additional description: Procedural intestinal perforation             |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Radius fracture                                 | Additional description: Radius fracture                               |                   |  |
| subjects affected / exposed                     | 9 / 1395 (0.65%)  | 12 / 1394 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 10  | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Rib fracture                                    | Additional description: Rib fracture                                  |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)  | 8 / 1394 (0.57%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 8             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Road traffic accident                           | Additional description: Road traffic accident                         |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Spinal fracture                                 | Additional description: Spinal fracture                               |                   |  |
| subjects affected / exposed                     | 9 / 1395 (0.65%)  | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 9   | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Sternal fracture                                | Additional description: Sternal fracture                              |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Subdural haematoma                              | Additional description: Subdural haematoma          |                   |  |
| subjects affected / exposed                     | 8 / 1395 (0.57%)                                    | 6 / 1394 (0.43%)  |  |
| occurrences causally related to treatment / all | 0 / 10  | 0 / 6             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Tendon rupture                                  | Additional description: Tendon rupture              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Thoracic vertebral fracture                     | Additional description: Thoracic vertebral fracture |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Tibia fracture                                  | Additional description: Tibia fracture              |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                    | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Toxicity to various agents                      | Additional description: Toxicity to various agents  |                   |  |
| subjects affected / exposed                     | 83 / 1395 (5.95%)                                   | 70 / 1394 (5.02%) |  |
| occurrences causally related to treatment / all | 26 / 88   | 8 / 78            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Traumatic fracture                              | Additional description: Traumatic fracture          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Traumatic haematoma                             | Additional description: Traumatic haematoma         |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Traumatic haemorrhage                           | Additional description: Traumatic haemorrhage       |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Ulna fracture                                   | Additional description: Ulna fracture           |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Upper limb fracture                             | Additional description: Upper limb fracture     |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Uterine rupture                                 | Additional description: Uterine rupture         |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Vascular pseudoaneurysm                         | Additional description: Vascular pseudoaneurysm |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Wrist fracture                                  | Additional description: Wrist fracture          |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Congenital, familial and genetic disorders      |   |                  |  |
| Atrial septal defect                            | Additional description: Atrial septal defect    |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hydrocele                                       | Additional description: Hydrocele               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Phimosis  | Additional description: Phimosis                |                  |  |



|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Syringomyelia                                   | Additional description: Syringomyelia               |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardiac disorders                               |   |                   |  |
| Acute coronary syndrome                         | Additional description: Acute coronary syndrome     |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Acute myocardial infarction                     | Additional description: Acute myocardial infarction |                   |  |
| subjects affected / exposed                     | 37 / 1395 (2.65%)                                   | 52 / 1394 (3.73%) |  |
| occurrences causally related to treatment / all | 0 / 46  | 0 / 63            |  |
| deaths causally related to treatment / all      | 0 / 2   | 0 / 3             |  |
| Angina pectoris                                 | Additional description: Angina pectoris             |                   |  |
| subjects affected / exposed                     | 49 / 1395 (3.51%)                                   | 37 / 1394 (2.65%) |  |
| occurrences causally related to treatment / all | 0 / 58  | 0 / 42            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Angina unstable                                 | Additional description: Angina unstable             |                   |  |
| subjects affected / exposed                     | 17 / 1395 (1.22%)                                   | 15 / 1394 (1.08%) |  |
| occurrences causally related to treatment / all | 0 / 19  | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Aortic valve stenosis                           | Additional description: Aortic valve stenosis       |                   |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)                                    | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 7   | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Arrhythmia                                      | Additional description: Arrhythmia                  |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                    | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 1 / 2   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Atrial fibrillation                             | Additional description: Atrial fibrillation         |                   |  |

|   |   |                        |  |
|---|---|------------------------|--|
| subjects affected / exposed                     | 314 / 1395<br>(22.51%)                                  | 308 / 1394<br>(22.09%) |  |
| occurrences causally related to treatment / all | 10 / 526  | 6 / 559                |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0                  |  |
| Atrial flutter                                  | Additional description: Atrial flutter                  |                        |  |
| subjects affected / exposed                     | 35 / 1395 (2.51%)                                       | 25 / 1394 (1.79%)      |  |
| occurrences causally related to treatment / all | 3 / 46  | 1 / 30                 |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0                  |  |
| Atrial tachycardia                              | Additional description: Atrial tachycardia              |                        |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)  | 6 / 1394 (0.43%)       |  |
| occurrences causally related to treatment / all | 1 / 9   | 1 / 8                  |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0                  |  |
| Atrioventricular block                          | Additional description: Atrioventricular block          |                        |  |
| subjects affected / exposed                     | 15 / 1395 (1.08%)                                       | 10 / 1394 (0.72%)      |  |
| occurrences causally related to treatment / all | 3 / 16  | 1 / 10                 |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0                  |  |
| Atrioventricular block complete                 | Additional description: Atrioventricular block complete |                        |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%)       |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0                  |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0                  |  |
| Bradycardia                                     | Additional description: Bradycardia                     |                        |  |
| subjects affected / exposed                     | 49 / 1395 (3.51%)                                       | 37 / 1394 (2.65%)      |  |
| occurrences causally related to treatment / all | 18 / 52   | 9 / 40                 |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0                  |  |
| Bundle branch block left                        | Additional description: Bundle branch block left        |                        |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%)       |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1                  |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0                  |  |
| Cardiac arrest                                  | Additional description: Cardiac arrest                  |                        |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)  | 6 / 1394 (0.43%)       |  |
| occurrences causally related to treatment / all | 1 / 7   | 1 / 6                  |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 2                  |  |
| Cardiac failure                                 | Additional description: Cardiac failure                 |                        |  |

|   |  |                        |  |
|---|--|------------------------|--|
| subjects affected / exposed                     | 140 / 1395<br>(10.04%)                             | 170 / 1394<br>(12.20%) |  |
| occurrences causally related to treatment / all | 3 / 222  | 0 / 297                |  |
| deaths causally related to treatment / all      | 0 / 15   | 0 / 9                  |  |
| Cardiac failure congestive                      | Additional description: Cardiac failure congestive |                        |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%)       |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0                  |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0                  |  |
| Cardiac tamponade                               | Additional description: Cardiac tamponade          |                        |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)                                   | 3 / 1394 (0.22%)       |  |
| occurrences causally related to treatment / all | 3 / 7  | 0 / 3                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Cardiogenic shock                               | Additional description: Cardiogenic shock          |                        |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)       |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Cardiomyopathy                                  | Additional description: Cardiomyopathy             |                        |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                   | 4 / 1394 (0.29%)       |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 4                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 2                  |  |
| Cardiovascular disorder                         | Additional description: Cardiovascular disorder    |                        |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)       |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Congestive cardiomyopathy                       | Additional description: Congestive cardiomyopathy  |                        |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                   | 1 / 1394 (0.07%)       |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 1                  |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0                  |  |
| Coronary artery disease                         | Additional description: Coronary artery disease    |                        |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 2 / 1394 (0.14%)       |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 2                  |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0                  |  |
| Intracardiac thrombus                           | Additional description: Intracardiac thrombus      |                        |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 5   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Ischaemic cardiomyopathy                        | Additional description: Ischaemic cardiomyopathy  |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                  | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 5   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Left ventricular failure                        | Additional description: Left ventricular failure  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Mitral valve disease                            | Additional description: Mitral valve disease      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Mitral valve incompetence                       | Additional description: Mitral valve incompetence |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 7 / 1394 (0.50%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 7             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Myocardial ischaemia                            | Additional description: Myocardial ischaemia      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Palpitations                                    | Additional description: Palpitations              |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                  | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 5   | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Pericardial effusion                            | Additional description: Pericardial effusion      |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 1 / 3   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Sinoatrial block                                | Additional description: Sinoatrial block          |                   |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Sinus node dysfunction                          | Additional description: Sinus node dysfunction           |                   |  |
| subjects affected / exposed                     | 37 / 1395 (2.65%)  | 35 / 1394 (2.51%) |  |
| occurrences causally related to treatment / all | 5 / 41   | 1 / 37            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Sinus tachycardia                               | Additional description: Sinus tachycardia                |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Stress cardiomyopathy                           | Additional description: Stress cardiomyopathy            |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1             |  |
| Supraventricular tachyarrhythmia                | Additional description: Supraventricular tachyarrhythmia |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Supraventricular tachycardia                    | Additional description: Supraventricular tachycardia     |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Torsade de pointes                              | Additional description: Torsade de pointes               |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Ventricular extrasystoles                       | Additional description: Ventricular extrasystoles        |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Ventricular fibrillation                        | Additional description: Ventricular fibrillation         |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                  | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 1            |  |
| Ventricular tachycardia                         | Additional description: Ventricular tachycardia   |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Nervous system disorders                        |   |                  |  |
| Amnesia   | Additional description: Amnesia                   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Basal ganglia haemorrhage                       | Additional description: Basal ganglia haemorrhage |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Brain injury                                    | Additional description: Brain injury              |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0            |  |
| Carotid artery stenosis                         | Additional description: Carotid artery stenosis   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Carpal tunnel syndrome                          | Additional description: Carpal tunnel syndrome    |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cerebral haemorrhage                            | Additional description: Cerebral haemorrhage      |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Cerebral infarction                             | Additional description: Cerebral infarction       |                  |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                               | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all           | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 1            |  |
| Cerebral small vessel ischaemic disease                   | Additional description: Cerebral small vessel ischaemic disease                   |                  |  |
| subjects affected / exposed                               | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all           | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 0            |  |
| Cerebrospinal fluid leakage                               | Additional description: Cerebrospinal fluid leakage                               |                  |  |
| subjects affected / exposed                               | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 0            |  |
| Cervicobrachial syndrome                                  | Additional description: Cervicobrachial syndrome                                  |                  |  |
| subjects affected / exposed                               | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 0            |  |
| Chronic inflammatory demyelinating polyradiculoneuropathy | Additional description: Chronic inflammatory demyelinating polyradiculoneuropathy |                  |  |
| subjects affected / exposed                               | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 4   | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 0            |  |
| Dementia  | Additional description: Dementia  |                  |  |
| subjects affected / exposed                               | 3 / 1395 (0.22%)  | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all           | 0 / 3   | 0 / 5            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 0            |  |
| Dementia with Lewy bodies                                 | Additional description: Dementia with Lewy bodies                                 |                  |  |
| subjects affected / exposed                               | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 0            |  |
| Diabetic hyperosmolar coma                                | Additional description: Diabetic hyperosmolar coma                                |                  |  |
| subjects affected / exposed                               | 1 / 1395 (0.07%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all           | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all                | 0 / 0   | 0 / 0            |  |
| Dizziness   | Additional description: Dizziness   |                  |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 6 / 1395 (0.43%)                                    | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Drug withdrawal headache                        | Additional description: Drug withdrawal headache    |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Embolic cerebral infarction                     | Additional description: Embolic cerebral infarction |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Encephalopathy                                  | Additional description: Encephalopathy              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Epilepsy  | Additional description: Epilepsy                    |                   |  |
| subjects affected / exposed                     | 8 / 1395 (0.57%)                                    | 9 / 1394 (0.65%)  |  |
| occurrences causally related to treatment / all | 0 / 9   | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Guillain-Barre syndrome                         | Additional description: Guillain-Barre syndrome     |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Haemorrhage intracranial                        | Additional description: Haemorrhage intracranial    |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Haemorrhagic stroke                             | Additional description: Haemorrhagic stroke         |                   |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)                                    | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 7   | 0 / 13            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 4             |  |
| Headache  | Additional description: Headache                    |                   |  |



|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Hydrocephalus                                   | Additional description: Hydrocephalus           |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Intercostal neuralgia                           | Additional description: Intercostal neuralgia   |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Intracranial aneurysm                           | Additional description: Intracranial aneurysm   |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Ischaemic stroke                                | Additional description: Ischaemic stroke        |                   |  |
| subjects affected / exposed                     | 32 / 1395 (2.29%)                               | 48 / 1394 (3.44%) |  |
| occurrences causally related to treatment / all | 0 / 35  | 0 / 51            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 4             |  |
| Migraine  | Additional description: Migraine                |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Multiple sclerosis                              | Additional description: Multiple sclerosis      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Multiple system atrophy                         | Additional description: Multiple system atrophy |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Myasthenia gravis                               | Additional description: Myasthenia gravis       |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Neuralgia                                       | Additional description: Neuralgia                     |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Neuritis  | Additional description: Neuritis                      |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Neurodegenerative disorder                      | Additional description: Neurodegenerative disorder    |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Neurological symptom                            | Additional description: Neurological symptom          |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Normal pressure hydrocephalus                   | Additional description: Normal pressure hydrocephalus |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Optic neuritis                                  | Additional description: Optic neuritis                |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Paraesthesia                                    | Additional description: Paraesthesia                  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Parkinson's disease                             | Additional description: Parkinson's disease           |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 6 / 1395 (0.43%)                                 | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 9  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Partial seizures                                | Additional description: Partial seizures         |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Peripheral nerve lesion                         | Additional description: Peripheral nerve lesion  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Piriformis syndrome                             | Additional description: Piriformis syndrome      |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Polyneuropathy                                  | Additional description: Polyneuropathy           |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                 | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 5  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Polyneuropathy alcoholic                        | Additional description: Polyneuropathy alcoholic |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Presyncope                                      | Additional description: Presyncope               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Sciatica  | Additional description: Sciatica                 |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Spinal cord compression                         | Additional description: Spinal cord compression  |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Spinal cord ischaemia                           | Additional description: Spinal cord ischaemia      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Spinal epidural haematoma                       | Additional description: Spinal epidural haematoma  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Subarachnoid haemorrhage                        | Additional description: Subarachnoid haemorrhage   |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 2             |  |
| Syncope   | Additional description: Syncope                    |                   |  |
| subjects affected / exposed                     | 62 / 1395 (4.44%)                                  | 46 / 1394 (3.30%) |  |
| occurrences causally related to treatment / all | 5 / 71   | 2 / 57            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Transient ischaemic attack                      | Additional description: Transient ischaemic attack |                   |  |
| subjects affected / exposed                     | 25 / 1395 (1.79%)                                  | 25 / 1394 (1.79%) |  |
| occurrences causally related to treatment / all | 0 / 25   | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Tremor  | Additional description: Tremor                     |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| VIIIth nerve lesion                             | Additional description: VIIIth nerve lesion        |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| VIth nerve disorder                             | Additional description: VIth nerve disorder        |                   |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| VIth nerve paralysis                            | Additional description: VIth nerve paralysis         |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| Blood and lymphatic system disorders            |  |                   |  |
| Agranulocytosis                                 | Additional description: Agranulocytosis              |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| Anaemia   | Additional description: Anaemia                      |                   |  |
| subjects affected / exposed                     | 15 / 1395 (1.08%)                                    | 19 / 1394 (1.36%) |  |
| occurrences causally related to treatment / all | 0 / 16   | 0 / 22            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| Anaemia of malignant disease                    | Additional description: Anaemia of malignant disease |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| Iron deficiency anaemia                         | Additional description: Iron deficiency anaemia      |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| Lymphadenopathy                                 | Additional description: Lymphadenopathy              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| Nephrogenic anaemia                             | Additional description: Nephrogenic anaemia          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| -----   |  |                   |  |
| Pancytopenia                                    | Additional description: Pancytopenia                 |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Thrombocytopenia                                | Additional description: Thrombocytopenia                |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Ear and labyrinth disorders                     |   |                  |  |
| Acute vestibular syndrome                       | Additional description: Acute vestibular syndrome       |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Deafness  | Additional description: Deafness                        |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Exostosis of external ear canal                 | Additional description: Exostosis of external ear canal |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)  | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Meniere's disease                               | Additional description: Meniere's disease               |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)  | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Vertigo   | Additional description: Vertigo                         |                  |  |
| subjects affected / exposed                     | 8 / 1395 (0.57%)  | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 8   | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Vertigo positional                              | Additional description: Vertigo positional              |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)  | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Vestibular disorder                             | Additional description: Vestibular disorder             |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Eye disorders                                   | Additional description: Age-related macular degeneration |                  |  |
| Age-related macular degeneration                |  |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Angle closure glaucoma                          | Additional description: Angle closure glaucoma           |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Entropion                                       | Additional description: Entropion                        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Eye haemorrhage                                 | Additional description: Eye haemorrhage                  |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Glaucoma  | Additional description: Glaucoma                         |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Retinal artery embolism                         | Additional description: Retinal artery embolism          |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Retinal artery occlusion                        | Additional description: Retinal artery occlusion         |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Retinal detachment                              | Additional description: Retinal detachment               |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Retinal vein occlusion                          | Additional description: Retinal vein occlusion |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                               | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Visual impairment                               | Additional description: Visual impairment      |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Gastrointestinal disorders                      |  |                   |  |
| Abdominal discomfort                            | Additional description: Abdominal discomfort   |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Abdominal hernia                                | Additional description: Abdominal hernia       |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                               | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Abdominal pain                                  | Additional description: Abdominal pain         |                   |  |
| subjects affected / exposed                     | 21 / 1395 (1.51%)                              | 12 / 1394 (0.86%) |  |
| occurrences causally related to treatment / all | 0 / 21   | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Abdominal pain upper                            | Additional description: Abdominal pain upper   |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Acute abdomen                                   | Additional description: Acute abdomen          |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1             |  |
| Cheilitis                                       | Additional description: Cheilitis              |                   |  |



|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Colitis   | Additional description: Colitis               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Colitis ischaemic                               | Additional description: Colitis ischaemic     |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Constipation                                    | Additional description: Constipation          |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                              | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Crohn's disease                                 | Additional description: Crohn's disease       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Diaphragmatic hernia                            | Additional description: Diaphragmatic hernia  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                              | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Diarrhoea                                       | Additional description: Diarrhoea             |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                              | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Diverticulum                                    | Additional description: Diverticulum          |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Duodenogastric reflux                           | Additional description: Duodenogastric reflux |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Dysphagia                                       | Additional description: Dysphagia                        |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Enteritis                                       | Additional description: Enteritis                        |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Enterocolitis                                   | Additional description: Enterocolitis                    |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Gastric haemorrhage                             | Additional description: Gastric haemorrhage              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Gastritis                                       | Additional description: Gastritis                        |                   |  |
| subjects affected / exposed                     | 12 / 1395 (0.86%)  | 10 / 1394 (0.72%) |  |
| occurrences causally related to treatment / all | 0 / 12   | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Gastrointestinal haemorrhage                    | Additional description: Gastrointestinal haemorrhage     |                   |  |
| subjects affected / exposed                     | 40 / 1395 (2.87%)  | 26 / 1394 (1.87%) |  |
| occurrences causally related to treatment / all | 0 / 46   | 0 / 28            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 1             |  |
| Gastrointestinal ischaemia                      | Additional description: Gastrointestinal ischaemia       |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1             |  |
| Gastrooesophageal reflux disease                | Additional description: Gastrooesophageal reflux disease |                   |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Haemoperitoneum                                 | Additional description: Haemoperitoneum              |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Haemorrhoids                                    | Additional description: Haemorrhoids                 |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hiatus hernia                                   | Additional description: Hiatus hernia                |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Ileus   | Additional description: Ileus                        |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                     | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1            |  |
| Inguinal hernia                                 | Additional description: Inguinal hernia              |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                     | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Inguinal hernia strangulated                    | Additional description: Inguinal hernia strangulated |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Intestinal fistula                              | Additional description: Intestinal fistula           |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Intestinal obstruction                          | Additional description: Intestinal obstruction       |                  |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Large intestine perforation                     | Additional description: Large intestine perforation   |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Large intestine polyp                           | Additional description: Large intestine polyp         |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Mallory-Weiss syndrome                          | Additional description: Mallory-Weiss syndrome        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Melaena   | Additional description: Melaena                       |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Mesenteric arterial occlusion                   | Additional description: Mesenteric arterial occlusion |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1            |  |
| Mesenteric artery embolism                      | Additional description: Mesenteric artery embolism    |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 2            |  |
| Mesenteric vein thrombosis                      | Additional description: Mesenteric vein thrombosis    |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Nausea  | Additional description: Nausea                        |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Oesophageal stenosis                            | Additional description: Oesophageal stenosis       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Oesophagitis                                    | Additional description: Oesophagitis               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pancreatitis                                    | Additional description: Pancreatitis               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pancreatitis acute                              | Additional description: Pancreatitis acute         |                  |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 5  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pancreatitis chronic                            | Additional description: Pancreatitis chronic       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Peptic ulcer                                    | Additional description: Peptic ulcer               |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Rectal haemorrhage                              | Additional description: Rectal haemorrhage         |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Salivary gland enlargement                      | Additional description: Salivary gland enlargement |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                             | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Short-bowel syndrome                            | Additional description: Short-bowel syndrome |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                             | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Subileus  | Additional description: Subileus             |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                             | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Umbilical hernia                                | Additional description: Umbilical hernia     |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                             | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Volvulus  | Additional description: Volvulus             |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                             | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Vomiting  | Additional description: Vomiting             |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                             | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Skin and subcutaneous tissue disorders          |  |                  |  |
| Decubitus ulcer                                 | Additional description: Decubitus ulcer      |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                             | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Dermatitis                                      | Additional description: Dermatitis           |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                             | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Diabetic foot                                   | Additional description: Diabetic foot        |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)                           | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 3                                      | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Eczema  | Additional description: Eczema             |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                           | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0                                      | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Erythema  | Additional description: Erythema           |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                           | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                      | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Granuloma annulare                              | Additional description: Granuloma annulare |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                           | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0                                      | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Pruritus  | Additional description: Pruritus           |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                           | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0                                      | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Psoriasis                                       | Additional description: Psoriasis          |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                           | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0                                      | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Skin lesion                                     | Additional description: Skin lesion        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                           | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0                                      | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Skin ulcer                                      | Additional description: Skin ulcer         |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                           | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 6                                      | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Urticaria                                       | Additional description: Urticaria          |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Renal and urinary disorders                     |  |                  |  |
| Acute kidney injury                             | Additional description: Acute kidney injury    |                  |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)                               | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Calculus bladder                                | Additional description: Calculus bladder       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Calculus urinary                                | Additional description: Calculus urinary       |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                               | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Chronic kidney disease                          | Additional description: Chronic kidney disease |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Cystitis haemorrhagic                           | Additional description: Cystitis haemorrhagic  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Haematuria                                      | Additional description: Haematuria             |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                               | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hydronephrosis                                  | Additional description: Hydronephrosis         |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                               | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Incontinence                                    | Additional description: Incontinence           |                  |  |



|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Nephrolithiasis                                 |   |                   |  |
|   | Additional description: Nephrolithiasis             |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                    | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Nephrotic syndrome                              |   |                   |  |
|   | Additional description: Nephrotic syndrome          |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Renal artery stenosis                           |   |                   |  |
|   | Additional description: Renal artery stenosis       |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Renal colic                                     |   |                   |  |
|   | Additional description: Renal colic                 |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Renal failure                                   |   |                   |  |
|   | Additional description: Renal failure               |                   |  |
| subjects affected / exposed                     | 21 / 1395 (1.51%)                                   | 21 / 1394 (1.51%) |  |
| occurrences causally related to treatment / all | 0 / 25  | 0 / 23            |  |
| deaths causally related to treatment / all      | 0 / 2   | 0 / 2             |  |
| Renal haemorrhage                               |   |                   |  |
|   | Additional description: Renal haemorrhage           |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Stress urinary incontinence                     |   |                   |  |
|   | Additional description: Stress urinary incontinence |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Urethral obstruction                            |   |                   |  |
|   | Additional description: Urethral obstruction        |                   |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Urinary incontinence                            | Additional description: Urinary incontinence               |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Urinary retention                               | Additional description: Urinary retention                  |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Urogenital haemorrhage                          | Additional description: Urogenital haemorrhage             |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Endocrine disorders                             |  |                  |  |
| Adrenal insufficiency                           | Additional description: Adrenal insufficiency              |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Adrenocortical insufficiency acute              | Additional description: Adrenocortical insufficiency acute |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Goitre  | Additional description: Goitre                             |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hyperadrenocorticism                            | Additional description: Hyperadrenocorticism               |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Hyperthyroidism                                 | Additional description: Hyperthyroidism                    |                  |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 6 / 1395 (0.43%)   | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 3 / 6  | 1 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Hypothyroidism                                  | Additional description: Hypothyroidism                               |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 3  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Inappropriate antidiuretic hormone secretion    | Additional description: Inappropriate antidiuretic hormone secretion |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Pituitary-dependent Cushing's syndrome          | Additional description: Pituitary-dependent Cushing's syndrome       |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Musculoskeletal and connective tissue disorders |  |                   |  |
| Arthralgia                                      | Additional description: Arthralgia                                   |                   |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)   | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 6  | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Arthritis                                       | Additional description: Arthritis                                    |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)   | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Back pain                                       | Additional description: Back pain                                    |                   |  |
| subjects affected / exposed                     | 24 / 1395 (1.72%)  | 16 / 1394 (1.15%) |  |
| occurrences causally related to treatment / all | 0 / 31   | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Bursitis  | Additional description: Bursitis                                     |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)   | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |

|   |  |                  |  |
|---|--|------------------|--|
| Cervical spinal stenosis                        | Additional description: Cervical spinal stenosis       |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Dupuytren's contracture                         | Additional description: Dupuytren's contracture        |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Exostosis                                       | Additional description: Exostosis                      |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Fistula   | Additional description: Fistula                        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                       | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Foot deformity                                  | Additional description: Foot deformity                 |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Groin pain                                      | Additional description: Groin pain                     |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Haemarthrosis                                   | Additional description: Haemarthrosis                  |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                       | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Intervertebral disc protrusion                  | Additional description: Intervertebral disc protrusion |                  |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                       | 7 / 1394 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 9  | 0 / 8            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Lumbar spinal stenosis                          | Additional description: Lumbar spinal stenosis         |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                   | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Musculoskeletal chest pain                      | Additional description: Musculoskeletal chest pain |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Musculoskeletal pain                            | Additional description: Musculoskeletal pain       |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Myalgia   | Additional description: Myalgia                    |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Osteoarthritis                                  | Additional description: Osteoarthritis             |                  |  |
| subjects affected / exposed                     | 7 / 1395 (0.50%)                                   | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 7  | 0 / 5            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Osteonecrosis                                   | Additional description: Osteonecrosis              |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Osteoporotic fracture                           | Additional description: Osteoporotic fracture      |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pain in extremity                               | Additional description: Pain in extremity          |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                   | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Pathological fracture                           | Additional description: Pathological fracture      |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Polyarthritis                                   | Additional description: Polyarthritis                |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Rhabdomyolysis                                  | Additional description: Rhabdomyolysis               |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Rheumatoid arthritis                            | Additional description: Rheumatoid arthritis         |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Scleroderma                                     | Additional description: Scleroderma                  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Spinal stenosis                                 | Additional description: Spinal stenosis              |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                     | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Spondylitis                                     | Additional description: Spondylitis                  |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Spondylolisthesis                               | Additional description: Spondylolisthesis            |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                     | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0            |  |
| Systemic lupus erythematosus                    | Additional description: Systemic lupus erythematosus |                  |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                            | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                       | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Infections and infestations                     |   |                  |  |
| Abdominal abscess                               | Additional description: Abdominal abscess   |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                            | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 2                                       | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Abscess   | Additional description: Abscess             |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                            | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3                                       | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Abscess bacterial                               | Additional description: Abscess bacterial   |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                            | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2                                       | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Anal abscess                                    | Additional description: Anal abscess        |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                            | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 0                                       | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Appendicitis                                    | Additional description: Appendicitis        |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                            | 7 / 1394 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 3                                       | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Arthritis bacterial                             | Additional description: Arthritis bacterial |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                            | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 2                                       | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Bacterial infection                             | Additional description: Bacterial infection |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                            | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                       | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0                                       | 0 / 0            |  |
| Bronchitis                                      | Additional description: Bronchitis          |                  |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                      | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cardiac infection                               | Additional description: Cardiac infection             |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Cellulitis                                      | Additional description: Cellulitis                    |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                      | 5 / 1394 (0.36%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 5             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Chronic sinusitis                               | Additional description: Chronic sinusitis             |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Clostridium difficile colitis                   | Additional description: Clostridium difficile colitis |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Creutzfeldt-Jakob disease                       | Additional description: Creutzfeldt-Jakob disease     |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0             |  |
| Device related infection                        | Additional description: Device related infection      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Diverticulitis                                  | Additional description: Diverticulitis                |                   |  |
| subjects affected / exposed                     | 15 / 1395 (1.08%)                                     | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 18  | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Ear infection                                   | Additional description: Ear infection                 |                   |  |



|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Emphyema  | Additional description: Emphyema                   |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Encephalitis                                    | Additional description: Encephalitis               |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Endocarditis                                    | Additional description: Endocarditis               |                   |  |
| subjects affected / exposed                     | 4 / 1395 (0.29%)                                   | 3 / 1394 (0.22%)  |  |
| occurrences causally related to treatment / all | 0 / 4  | 0 / 3             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 1             |  |
| Epididymitis                                    | Additional description: Epididymitis               |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                   | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Erysipelas                                      | Additional description: Erysipelas                 |                   |  |
| subjects affected / exposed                     | 15 / 1395 (1.08%)                                  | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 19   | 0 / 15            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0             |  |
| Gastroenteritis                                 | Additional description: Gastroenteritis            |                   |  |
| subjects affected / exposed                     | 9 / 1395 (0.65%)                                   | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 10   | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Gastrointestinal infection                      | Additional description: Gastrointestinal infection |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                   | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Groin abscess                                   | Additional description: Groin abscess              |                   |  |

|   |  |                   |  |
|---|--|-------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                 | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 1 / 2  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Herpes zoster                                   | Additional description: Herpes zoster            |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                 | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 2  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Infection                                       | Additional description: Infection                |                   |  |
| subjects affected / exposed                     | 14 / 1395 (1.00%)                                | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 16   | 0 / 11            |  |
| deaths causally related to treatment / all      | 0 / 1  | 0 / 0             |  |
| Intervertebral discitis                         | Additional description: Intervertebral discitis  |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Localised infection                             | Additional description: Localised infection      |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Mediastinitis                                   | Additional description: Mediastinitis            |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                 | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1  | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Muscle abscess                                  | Additional description: Muscle abscess           |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Oesophageal candidiasis                         | Additional description: Oesophageal candidiasis  |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                 | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0  | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0  | 0 / 0             |  |
| Ophthalmic herpes zoster                        | Additional description: Ophthalmic herpes zoster |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Osteomyelitis                                   | Additional description: Osteomyelitis             |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Otitis media                                    | Additional description: Otitis media              |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Paronychia                                      | Additional description: Paronychia                |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Peritonitis                                     | Additional description: Peritonitis               |                   |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                                  | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Pharyngitis                                     | Additional description: Pharyngitis               |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Pneumonia                                       | Additional description: Pneumonia                 |                   |  |
| subjects affected / exposed                     | 69 / 1395 (4.95%)                                 | 81 / 1394 (5.81%) |  |
| occurrences causally related to treatment / all | 1 / 90  | 1 / 106           |  |
| deaths causally related to treatment / all      | 0 / 7   | 1 / 9             |  |
| Post procedural infection                       | Additional description: Post procedural infection |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                  | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Pyelonephritis                                  | Additional description: Pyelonephritis            |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Pyelonephritis acute                            | Additional description: Pyelonephritis acute        |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Respiratory tract infection                     | Additional description: Respiratory tract infection |                   |  |
| subjects affected / exposed                     | 9 / 1395 (0.65%)                                    | 13 / 1394 (0.93%) |  |
| occurrences causally related to treatment / all | 0 / 9   | 0 / 14            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0             |  |
| Rotavirus infection                             | Additional description: Rotavirus infection         |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                    | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Sepsis  | Additional description: Sepsis                      |                   |  |
| subjects affected / exposed                     | 13 / 1395 (0.93%)                                   | 17 / 1394 (1.22%) |  |
| occurrences causally related to treatment / all | 0 / 14  | 0 / 17            |  |
| deaths causally related to treatment / all      | 0 / 7   | 0 / 7             |  |
| Septic encephalopathy                           | Additional description: Septic encephalopathy       |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                    | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Septic shock                                    | Additional description: Septic shock                |                   |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                                    | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 3             |  |
| Skin bacterial infection                        | Additional description: Skin bacterial infection    |                   |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)                                    | 4 / 1394 (0.29%)  |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 4             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Staphylococcal sepsis                           | Additional description: Staphylococcal sepsis       |                   |  |

|   |   |                   |  |
|---|---|-------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0             |  |
| Tick-borne viral encephalitis                   | Additional description: Tick-borne viral encephalitis |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Tooth abscess                                   | Additional description: Tooth abscess                 |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 0 / 1394 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Tuberculosis                                    | Additional description: Tuberculosis                  |                   |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                                      | 1 / 1394 (0.07%)  |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 1             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Urinary tract infection                         | Additional description: Urinary tract infection       |                   |  |
| subjects affected / exposed                     | 27 / 1395 (1.94%)                                     | 19 / 1394 (1.36%) |  |
| occurrences causally related to treatment / all | 0 / 35  | 0 / 21            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Urosepsis                                       | Additional description: Urosepsis                     |                   |  |
| subjects affected / exposed                     | 6 / 1395 (0.43%)                                      | 9 / 1394 (0.65%)  |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 10            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 1             |  |
| Viral infection                                 | Additional description: Viral infection               |                   |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                                      | 2 / 1394 (0.14%)  |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 2             |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0             |  |
| Wound infection                                 | Additional description: Wound infection               |                   |  |
| subjects affected / exposed                     | 5 / 1395 (0.36%)                                      | 11 / 1394 (0.79%) |  |
| occurrences causally related to treatment / all | 0 / 6   | 0 / 12            |  |
| deaths causally related to treatment / all      | 0 / 1   | 0 / 0             |  |
| Metabolism and nutrition disorders              |   |                   |  |
| Dehydration                                     | Additional description: Dehydration                   |                   |  |

|   |   |                  |  |
|---|---|------------------|--|
| subjects affected / exposed                     | 4 / 1395 (0.29%)                              | 4 / 1394 (0.29%) |  |
| occurrences causally related to treatment / all | 0 / 4   | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Diabetes mellitus                               | Additional description: Diabetes mellitus     |                  |  |
| subjects affected / exposed                     | 0 / 1395 (0.00%)                              | 7 / 1394 (0.50%) |  |
| occurrences causally related to treatment / all | 0 / 0   | 0 / 7            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Dyslipidaemia                                   | Additional description: Dyslipidaemia         |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                              | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Electrolyte imbalance                           | Additional description: Electrolyte imbalance |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                              | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Gout  | Additional description: Gout                  |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                              | 5 / 1394 (0.36%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hyperglycaemia                                  | Additional description: Hyperglycaemia        |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                              | 3 / 1394 (0.22%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 4            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hyperkalaemia                                   | Additional description: Hyperkalaemia         |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                              | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2   | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hypoglycaemia                                   | Additional description: Hypoglycaemia         |                  |  |
| subjects affected / exposed                     | 3 / 1395 (0.22%)                              | 2 / 1394 (0.14%) |  |
| occurrences causally related to treatment / all | 0 / 3   | 0 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0   | 0 / 0            |  |
| Hypokalaemia                                    | Additional description: Hypokalaemia          |                  |  |

|   |  |                  |  |
|---|--|------------------|--|
| subjects affected / exposed                     | 1 / 1395 (0.07%)                           | 1 / 1394 (0.07%) |  |
| occurrences causally related to treatment / all | 0 / 3                                      | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Hyponatraemia                                   | Additional description: Hyponatraemia      |                  |  |
| subjects affected / exposed                     | 2 / 1395 (0.14%)                           | 6 / 1394 (0.43%) |  |
| occurrences causally related to treatment / all | 0 / 2                                      | 0 / 6            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |
| Metabolic acidosis                              | Additional description: Metabolic acidosis |                  |  |
| subjects affected / exposed                     | 1 / 1395 (0.07%)                           | 0 / 1394 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1                                      | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0                                      | 0 / 0            |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | Early rhythm control | Usual care       |  |
|---|----------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                      |                  |  |
| subjects affected / exposed                           | 0 / 1395 (0.00%)     | 0 / 1394 (0.00%) |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 10 December 2010 | Essential changes in inclusion criteria              |
| 09 December 2011 | essential changes and administrative changes         |
| 14 May 2015      | essential changes and further administrative changes |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported