



## Clinical trial results:

### A Phase 3, Multicenter Study to Evaluate the Long-Term Safety and Efficacy of Baricitinib in Patients with Rheumatoid Arthritis

#### Summary

|                          |  |
|--------------------------|--|
| EudraCT number           | 2012-003686-17   |
| Trial protocol           | IT SK CZ BE PL SE GB HU AT DK DE PT NL ES LV LT GR SI HR |
| Global end of trial date | 15 November 2020   |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v2 (current)     |
| This version publication date  | 15 May 2022      |
| First version publication date | 27 November 2021 |

|                         |   |
|-------------------------|---|
| Version creation reason | <ul style="list-style-type: none"><li>New data added to full data set</li><li>New data added to full data set</li></ul> |
|-------------------------|---|

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | I4V-MC-JADY |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                     |
|------------------------------------|---------------------|
| ISRCTN number                      | -                   |
| ClinicalTrials.gov id (NCT number) | NCT01885078         |
| WHO universal trial number (UTN)   | -                   |
| Other trial identifiers            | Trial Number: 14060 |

Notes:

#### Sponsors

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

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 12 November 2020 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 12 November 2020 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the long-term safety and tolerability of baricitinib.

Protection of trial subjects:

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

Background therapy:

Participants may continue to receive the background non-investigational, open-label conventional disease-modifying antirheumatic drugs (cDMARD), nonsteroidal anti-inflammatory drug (NSAID), corticosteroid, and other analgesic therapies they were receiving at completion of the originating study.

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 27 June 2013 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 72 |
| Country: Number of subjects enrolled | Netherlands: 1         |
| Country: Number of subjects enrolled | Poland: 156            |
| Country: Number of subjects enrolled | Portugal: 11           |
| Country: Number of subjects enrolled | Slovakia: 27           |
| Country: Number of subjects enrolled | Slovenia: 5            |
| Country: Number of subjects enrolled | Spain: 86              |
| Country: Number of subjects enrolled | Sweden: 3              |
| Country: Number of subjects enrolled | United Kingdom: 26     |
| Country: Number of subjects enrolled | Croatia: 9             |
| Country: Number of subjects enrolled | Austria: 17            |
| Country: Number of subjects enrolled | Belgium: 41            |
| Country: Number of subjects enrolled | Czechia: 56            |
| Country: Number of subjects enrolled | Denmark: 5             |
| Country: Number of subjects enrolled | France: 36             |
| Country: Number of subjects enrolled | Germany: 36            |
| Country: Number of subjects enrolled | Greece: 8              |
| Country: Number of subjects enrolled | Hungary: 60            |

|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Italy: 27               |
| Country: Number of subjects enrolled | Latvia: 8               |
| Country: Number of subjects enrolled | Lithuania: 21           |
| Country: Number of subjects enrolled | United States: 488      |
| Country: Number of subjects enrolled | Canada: 47              |
| Country: Number of subjects enrolled | Argentina: 430          |
| Country: Number of subjects enrolled | Australia: 32           |
| Country: Number of subjects enrolled | Brazil: 30              |
| Country: Number of subjects enrolled | India: 71               |
| Country: Number of subjects enrolled | Israel: 27              |
| Country: Number of subjects enrolled | China: 208              |
| Country: Number of subjects enrolled | Japan: 328              |
| Country: Number of subjects enrolled | Mexico: 214             |
| Country: Number of subjects enrolled | Romania: 21             |
| Country: Number of subjects enrolled | Russian Federation: 122 |
| Country: Number of subjects enrolled | South Africa: 56        |
| Country: Number of subjects enrolled | Taiwan: 81              |
| Country: Number of subjects enrolled | Switzerland: 7          |
| Country: Number of subjects enrolled | Turkey: 3               |
| Worldwide total number of subjects   | 2876                    |
| EEA total number of subjects         | 634                     |

Notes:

### Subjects enrolled per age group

|   |      |
|---|------|
| In utero                                  | 0    |
| Preterm newborn - gestational age < 37 wk | 0    |
| Newborns (0-27 days)                      | 0    |
| Infants and toddlers (28 days-23 months)  | 0    |
| Children (2-11 years)                     | 0    |
| Adolescents (12-17 years)                 | 0    |
| Adults (18-64 years)                      | 2358 |
| From 65 to 84 years                       | 517  |
| 85 years and over                         | 1    |

## Subject disposition

### Recruitment

Recruitment details:

Participants were eligible to participate in the Step-down period if they achieved a sustained (at least 3 months in JADY) low disease activity (CDAI score  $\leq 10$ ; for participants originating in Studies JADV, JADX, JADW, and JAGS) or sustained remission (CDAI score  $\leq 2.8$ ; for participants originating in Study JADZ).

### Pre-assignment

Screening details:

Participants who completed an originating study: I4V-MC-JADZ (NCT01711359), I4V-MC-JADV (NCT01710358), I4V-MC-JADX (NCT01721057), I4V-MC-JADW (NCT01721044), I4V-MC-JADA (NCT01185353), or I4V-MC-JAGS (NCT02265705) were eligible for enrollment into study JADY.

### Period 1

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

### Arms

|                              |                       |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes                   |
| <b>Arm title</b>             | JADZ 4 mg Baricitinib |

Arm description:

4 mg Baricitinib administered orally once daily.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Baricitinib  |
| Investigational medicinal product code | LY3009104    |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

4 mg Baricitinib administered orally once daily.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | JADV 4 mg Baricitinib |
|------------------|-----------------------|

Arm description:

4 mg Baricitinib administered orally once daily.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Baricitinib  |
| Investigational medicinal product code | LY3009104    |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

4 mg Baricitinib administered orally once daily.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | JADX 2 mg Baricitinib |
|------------------|-----------------------|

Arm description:

2 mg Baricitinib administered orally once daily

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                       |
|--|-----------------------|
| Investigational medicinal product name   | Baricitinib           |
| Investigational medicinal product code   | LY3009104             |
| Other name   |                       |
| Pharmaceutical forms   | Tablet                |
| Routes of administration   | Oral use              |
| Dosage and administration details:<br>2 mg Baricitinib administered orally once daily. |                       |
| <b>Arm title</b>   | JADX 4 mg Baricitinib |
| Arm description:<br>4 mg Baricitinib administered orally once daily.                   |                       |
| Arm type   | Experimental          |
| Investigational medicinal product name   | Baricitinib           |
| Investigational medicinal product code   | LY3009104             |
| Other name   |                       |
| Pharmaceutical forms   | Tablet                |
| Routes of administration   | Oral use              |
| Dosage and administration details:<br>4 mg Baricitinib administered orally once daily. |                       |
| <b>Arm title</b>   | JADW 2 mg Baricitinib |
| Arm description:<br>2 mg Baricitinib administered orally once daily.                   |                       |
| Arm type   | Experimental          |
| Investigational medicinal product name   | Baricitinib           |
| Investigational medicinal product code   | LY3009104             |
| Other name   |                       |
| Pharmaceutical forms   | Tablet                |
| Routes of administration   | Oral use              |
| Dosage and administration details:<br>2 mg Baricitinib administered orally once daily. |                       |
| <b>Arm title</b>   | JADW 4 mg Baricitinib |
| Arm description:<br>4 mg Baricitinib administered orally once daily.                   |                       |
| Arm type   | Experimental          |
| Investigational medicinal product name   | Baricitinib           |
| Investigational medicinal product code   | LY3009104             |
| Other name   |                       |
| Pharmaceutical forms   | Tablet                |
| Routes of administration   | Oral use              |
| Dosage and administration details:<br>4 mg Baricitinib administered orally once daily. |                       |
| Investigational medicinal product name   | Baricitinib           |
| Investigational medicinal product code   | LY3009104             |
| Other name   |                       |
| Pharmaceutical forms   | Tablet                |
| Routes of administration   | Oral use              |
| Dosage and administration details:<br>4 mg Baricitinib administered orally once daily. |                       |
| <b>Arm title</b>   | JAGS 4 mg Baricitinib |
| Arm description:<br>4 mg Baricitinib administered orally once daily.                   |                       |

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Baricitinib  |
| Investigational medicinal product code | LY3009104    |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

4 mg Baricitinib administered orally once daily.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | JADA 4 mg Baricitinib |
|------------------|-----------------------|

Arm description:

4 mg Baricitinib administered orally once daily.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Baricitinib  |
| Investigational medicinal product code | LY3009104    |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

4 mg Baricitinib administered orally once daily.

| <b>Number of subjects in period 1</b>    | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|
| Started                                  | 451                   | 1090                  | 180                   |
| Received at Least One Dose of Study Drug | 451                   | 1090                  | 180                   |
| Completed                                | 19                    | 64                    | 49                    |
| Not completed                            | 432                   | 1026                  | 131                   |
| Physician decision                       | 19                    | 21                    | 5                     |
| Consent withdrawn by subject             | 72                    | 131                   | 25                    |
| Adverse event, non-fatal                 | 52                    | 136                   | 30                    |
| Death                                    | 13                    | 33                    | 5                     |
| Unknown                                  | -                     | -                     | -                     |
| Lost to follow-up                        | 16                    | 19                    | 7                     |
| Sponsor decision                         | 245                   | 648                   | 49                    |
| Lack of efficacy                         | 12                    | 33                    | 10                    |
| Protocol deviation                       | 3                     | 5                     | -                     |

| <b>Number of subjects in period 1</b>    | JADX 4 mg Baricitinib | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|
| Started                                  | 403                   | 117                   | 331                   |
| Received at Least One Dose of Study Drug | 403                   | 117                   | 331                   |
| Completed                                | 120                   | 27                    | 81                    |
| Not completed                            | 283                   | 90                    | 250                   |
| Physician decision                       | 12                    | 9                     | 24                    |
| Consent withdrawn by subject             | 63                    | 15                    | 34                    |

|                          |    |    |    |
|--------------------------|----|----|----|
| Adverse event, non-fatal | 73 | 17 | 72 |
| Death                    | 9  | 2  | 10 |
| Unknown                  | 1  | -  | -  |
| Lost to follow-up        | 9  | 2  | 8  |
| Sponsor decision         | 90 | 20 | 38 |
| Lack of efficacy         | 23 | 24 | 58 |
| Protocol deviation       | 3  | 1  | 6  |

| Number of subjects in period 1           | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|--|-----------------------|-----------------------|
| Started                                  | 221                   | 83                    |
| Received at Least One Dose of Study Drug | 221                   | 83                    |
| Completed                                | 0                     | 55                    |
| Not completed                            | 221                   | 28                    |
| Physician decision                       | 4                     | 3                     |
| Consent withdrawn by subject             | 17                    | 10                    |
| Adverse event, non-fatal                 | 24                    | 5                     |
| Death                                    | 3                     | 2                     |
| Unknown                                  | -                     | -                     |
| Lost to follow-up                        | 2                     | -                     |
| Sponsor decision                         | 162                   | 3                     |
| Lack of efficacy                         | 9                     | 5                     |
| Protocol deviation                       | -                     | -                     |

## Period 2

|                              |  |
|------------------------------|--|
| Period 2 title               | Step-down                              |
| Is this the baseline period? | No                                     |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

## Arms

|  |                            |
|--|----------------------------|
| Are arms mutually exclusive?           | No                         |
| <b>Arm title</b>                       | 2 mg Baricitinib Step-down |
| Arm description: -                     |                            |
| Arm type                               | Experimental               |
| Investigational medicinal product name | Baricitinib                |
| Investigational medicinal product code | LY3009104                  |
| Other name                             |                            |
| Pharmaceutical forms                   | Tablet                     |
| Routes of administration               | Oral use                   |

Dosage and administration details:

2 mg Baricitinib administered orally once daily in the Step-down period.

|  |                            |
|--|----------------------------|
| <b>Arm title</b>                       | 4 mg Baricitinib Step-down |
| Arm description: -                     |                            |
| Arm type                               | Experimental               |
| Investigational medicinal product name | Baricitinib                |
| Investigational medicinal product code | LY3009104                  |
| Other name                             |                            |
| Pharmaceutical forms                   | Tablet                     |
| Routes of administration               | Oral use                   |

Dosage and administration details:

4 mg Baricitinib administered orally once daily in the Step-down period.

| <b>Number of subjects in period 2</b> | 2 mg Baricitinib<br>Step-down | 4 mg Baricitinib<br>Step-down |
|---------------------------------------|-------------------------------|-------------------------------|
| Started                               | 592                           | 594                           |
| Completed                             | 523                           | 533                           |
| Not completed                         | 69                            | 61                            |
| Consent withdrawn by subject          | 25                            | 15                            |
| Physician decision                    | 7                             | 2                             |
| Adverse event, non-fatal              | 29                            | 38                            |
| Death                                 | 4                             | 3                             |
| Sponsor decision                      | 1                             | 1                             |
| Lost to follow-up                     | 1                             | 1                             |
| Lack of efficacy                      | 1                             | -                             |
| Protocol deviation                    | 1                             | 1                             |



## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Treatment Period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values                    | Treatment Period | Total |  |
|---|------------------|-------|--|
| Number of subjects                        | 2876             | 2876  |  |
| Age categorical                           |                  |       |  |
| Units: Subjects                           |                  |       |  |
| Adults (18-64 years)                      | 2358             | 2358  |  |
| From 65-84 years                          | 517              | 517   |  |
| 85 years and over                         | 1                | 1     |  |
| Gender categorical                        |                  |       |  |
| Units: Subjects                           |                  |       |  |
| Female                                    | 2262             | 2262  |  |
| Male                                      | 614              | 614   |  |
| Race                                      |                  |       |  |
| Units: Subjects                           |                  |       |  |
| American Indian or Alaska Native          | 143              | 143   |  |
| Asian                                     | 781              | 781   |  |
| Native Hawaiian or Other Pacific Islander | 1                | 1     |  |
| Black or African American                 | 64               | 64    |  |
| White                                     | 1859             | 1859  |  |
| More than one race                        | 23               | 23    |  |
| Unknown or Not Reported                   | 5                | 5     |  |
| Region of Enrollment                      |                  |       |  |
| Units: Subjects                           |                  |       |  |
| United States                             | 488              | 488   |  |
| Czechia                                   | 56               | 56    |  |
| Portugal                                  | 11               | 11    |  |
| Russia                                    | 122              | 122   |  |
| Greece                                    | 8                | 8     |  |
| South Korea                               | 72               | 72    |  |
| Latvia                                    | 8                | 8     |  |
| Sweden                                    | 3                | 3     |  |
| Austria                                   | 17               | 17    |  |
| Netherlands                               | 1                | 1     |  |
| China                                     | 208              | 208   |  |
| Poland                                    | 156              | 156   |  |
| Brazil                                    | 30               | 30    |  |
| Slovenia                                  | 5                | 5     |  |
| Slovakia                                  | 27               | 27    |  |
| France                                    | 36               | 36    |  |
| Lithuania                                 | 21               | 21    |  |
| Croatia                                   | 9                | 9     |  |
| Argentina                                 | 430              | 430   |  |
| Romania                                   | 21               | 21    |  |

|                |     |     |  |
|----------------|-----|-----|--|
| Hungary        | 60  | 60  |  |
| Japan          | 328 | 328 |  |
| United Kingdom | 26  | 26  |  |
| Switzerland    | 7   | 7   |  |
| India          | 71  | 71  |  |
| Spain          | 86  | 86  |  |
| Canada         | 47  | 47  |  |
| Turkey         | 3   | 3   |  |
| Belgium        | 41  | 41  |  |
| Taiwan         | 81  | 81  |  |
| Denmark        | 5   | 5   |  |
| South Africa   | 56  | 56  |  |
| Italy          | 27  | 27  |  |
| Mexico         | 214 | 214 |  |
| Israel         | 27  | 27  |  |
| Australia      | 32  | 32  |  |
| Germany        | 36  | 36  |  |

### Subject analysis sets

|   |                             |
|---|-----------------------------|
| Subject analysis set title  | 2 mg Baricitinib            |
| Subject analysis set type   | Modified intention-to-treat |
| Subject analysis set description:<br>2 mg Baricitinib administered orally once daily. |                             |
| Subject analysis set title  | 4 mg Baricitinib            |
| Subject analysis set type   | Modified intention-to-treat |
| Subject analysis set description:<br>4 mg Baricitinib administered orally once daily. |                             |

| Reporting group values                    | 2 mg Baricitinib | 4 mg Baricitinib |  |
|---|------------------|------------------|--|
| Number of subjects                        | 297              | 2579             |  |
| Age categorical                           |                  |                  |  |
| Units: Subjects                           |                  |                  |  |
| Adults (18-64 years)                      | 236              | 2122             |  |
| From 65-84 years                          | 61               | 456              |  |
| 85 years and over                         | 0                | 1                |  |
| Gender categorical                        |                  |                  |  |
| Units: Subjects                           |                  |                  |  |
| Female                                    | 231              | 2031             |  |
| Male                                      | 66               | 548              |  |
| Race                                      |                  |                  |  |
| Units: Subjects                           |                  |                  |  |
| American Indian or Alaska Native          | 7                | 136              |  |
| Asian                                     | 56               | 725              |  |
| Native Hawaiian or Other Pacific Islander | 0                | 1                |  |
| Black or African American                 | 16               | 48               |  |
| White                                     | 217              | 1642             |  |
| More than one race                        | 1                | 22               |  |
| Unknown or Not Reported                   | 0                | 5                |  |
| Region of Enrollment                      |                  |                  |  |

| Units: Subjects |    |     |  |
|-----------------|----|-----|--|
| United States   | 91 | 397 |  |
| Czechia         | 3  | 53  |  |
| Portugal        | 2  | 9   |  |
| Russia          | 10 | 112 |  |
| Greece          | 2  | 6   |  |
| South Korea     | 9  | 63  |  |
| Latvia          | 0  | 8   |  |
| Sweden          | 0  | 3   |  |
| Austria         | 3  | 14  |  |
| Netherlands     | 1  | 0   |  |
| China           | 0  | 208 |  |
| Poland          | 20 | 136 |  |
| Brazil          | 0  | 30  |  |
| Slovenia        | 0  | 5   |  |
| Slovakia        | 3  | 24  |  |
| France          | 6  | 30  |  |
| Lithuania       | 0  | 21  |  |
| Croatia         | 2  | 7   |  |
| Argentina       | 12 | 412 |  |
| Romania         | 2  | 19  |  |
| Hungary         | 8  | 52  |  |
| Japan           | 7  | 321 |  |
| United Kingdom  | 4  | 22  |  |
| Switzerland     | 0  | 7   |  |
| India           | 16 | 55  |  |
| Spain           | 15 | 71  |  |
| Canada          | 11 | 36  |  |
| Turkey          | 1  | 2   |  |
| Belgium         | 3  | 38  |  |
| Taiwan          | 23 | 58  |  |
| Denmark         | 2  | 3   |  |
| South Africa    | 0  | 56  |  |
| Italy           | 6  | 21  |  |
| Mexico          | 13 | 201 |  |
| Israel          | 6  | 21  |  |
| Australia       | 6  | 26  |  |
| Germany         | 4  | 32  |  |

## End points

### End points reporting groups

|   |                             |
|---|-----------------------------|
| Reporting group title   | JADZ 4 mg Baricitinib       |
| Reporting group description:<br>4 mg Baricitinib administered orally once daily.      |                             |
| Reporting group title   | JADV 4 mg Baricitinib       |
| Reporting group description:<br>4 mg Baricitinib administered orally once daily.      |                             |
| Reporting group title   | JADX 2 mg Baricitinib       |
| Reporting group description:<br>2 mg Baricitinib administered orally once daily       |                             |
| Reporting group title   | JADX 4 mg Baricitinib       |
| Reporting group description:<br>4 mg Baricitinib administered orally once daily.      |                             |
| Reporting group title   | JADW 2 mg Baricitinib       |
| Reporting group description:<br>2 mg Baricitinib administered orally once daily.      |                             |
| Reporting group title   | JADW 4 mg Baricitinib       |
| Reporting group description:<br>4 mg Baricitinib administered orally once daily.      |                             |
| Reporting group title   | JAGS 4 mg Baricitinib       |
| Reporting group description:<br>4 mg Baricitinib administered orally once daily.      |                             |
| Reporting group title   | JADA 4 mg Baricitinib       |
| Reporting group description:<br>4 mg Baricitinib administered orally once daily.      |                             |
| Reporting group title   | 2 mg Baricitinib Step-down  |
| Reporting group description: -  |                             |
| Reporting group title   | 4 mg Baricitinib Step-down  |
| Reporting group description: -  |                             |
| Subject analysis set title  | 2 mg Baricitinib            |
| Subject analysis set type   | Modified intention-to-treat |
| Subject analysis set description:<br>2 mg Baricitinib administered orally once daily. |                             |
| Subject analysis set title  | 4 mg Baricitinib            |
| Subject analysis set type   | Modified intention-to-treat |
| Subject analysis set description:<br>4 mg Baricitinib administered orally once daily. |                             |

### Primary: Number of Participants Who Experienced Adverse Events (AEs) or Serious AE

|  |  |
|--|--|
| End point title  | Number of Participants Who Experienced Adverse Events (AEs) or Serious AE <sup>[1]</sup> |
| End point description:<br>An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can be any unfavorable and unintended sign (i.e., abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. Non-serious AEs are reported at a threshold of 5%.<br><br>An SAE is an AE from this study that results in any of the following: death, initial or prolonged inpatient |  |

hospitalization, a life-threatening experience, persistent or significant disability/incapacity, congenital anomaly/birth defect, considered significant by the investigator for any other reason

A summary of serious adverse events (SAEs) and other non-serious adverse events (AEs), regardless of causality, were reported in the Reported Adverse Events module.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline through 84 Months

Analysis Population Description (APD): All enrolled participants who received at least 1 dose of study drug and did not discontinue the study for the reason 'Lost to Follow-up' at the first postbaseline visit in study JADY.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical comparison was not conducted on safety outcome measure.

| End point values             | 2 mg Baricitinib Step-down | 4 mg Baricitinib Step-down | 2 mg Baricitinib     | 4 mg Baricitinib     |
|------------------------------|----------------------------|----------------------------|----------------------|----------------------|
| Subject group type           | Reporting group            | Reporting group            | Subject analysis set | Subject analysis set |
| Number of subjects analysed  | 592                        | 594                        | 297                  | 2579                 |
| Units: Count of participants |                            |                            |                      |                      |
| Adverse Events               | 270                        | 315                        | 234                  | 1532                 |
| Serious Adverse Events       | 164                        | 178                        | 112                  | 517                  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining an American College of Rheumatology (ACR) Response of ACR20

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining an American College of Rheumatology (ACR) Response of ACR20 |
|-----------------|--|

End point description:

ACR20 Responder Index is a composite of clinical, laboratory, and functional measures in rheumatoid arthritis (RA). An ACR20 Responder is a participant who had  $\geq 20\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 20\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, Health Assessment Questionnaire-Disability Index (HAQ-DI) (assessment of participant's physical function), pain due to RA, and hsCRP. Percentage of participants achieving ACR20 response = (number of ACR20 responders) / (number of participants analyzed) \* 100

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 1, 3 and 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of Participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 92.6 (89.7 to 94.7)   | 88.4 (86.3 to 90.2)   | 79.3 (72.6 to 84.7)   | 79.5 (75.1 to 83.3)   |
| Year 3                            | 78.3 (74.1 to 82.0)   | 76.6 (73.9 to 79.1)   | 71.6 (64.4 to 77.9)   | 70.5 (65.6 to 74.9)   |
| Year 5                            | 67.3 (62.7 to 71.6)   | 65.6 (62.6 to 68.4)   | 60.4 (52.8 to 67.4)   | 56.0 (50.9 to 61.0)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of Participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 72.3 (62.9 to 80.1)   | 70.8 (65.2 to 75.9)   | 86.7 (81.4 to 90.6)   | 75.6 (65.1 to 83.8)   |
| Year 3                            | 57.4 (47.7 to 66.6)   | 55.8 (49.9 to 61.6)   | 73.8 (67.5 to 79.3)   | 71.8 (61.0 to 80.6)   |
| Year 5                            | 50.5 (40.9 to 60.0)   | 43.1 (37.3 to 49.0)   | 24.8 (19.4 to 31.0)   | 60.3 (49.2 to 70.4)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining an American College of Rheumatology (ACR) Response of ACR50

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining an American College of Rheumatology (ACR) Response of ACR50 |
|-----------------|--|

End point description:

ACR 50 Responder Index is a composite of clinical, laboratory, and functional measures in rheumatoid arthritis (RA). An ACR50 Responder is a participant who had  $\geq 50\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 50\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, Health Assessment Questionnaire-Disability Index (HAQ-DI) (assessment of participant's physical function), pain due to RA, and hsCRP. Percentage of participants achieving ACR20 response = (number of ACR50 responders) / (number of participants analyzed) \* 100

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

End point timeframe:

Year 1, 3 and 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 80.0 (75.9 to 83.5)   | 67.7 (64.8 to 70.5)   | 58.0 (50.5 to 65.2)   | 58.2 (53.1 to 63.1)   |
| Year 3                            | 67.8 (63.2 to 72.1)   | 61.6 (58.6 to 64.5)   | 49.7 (42.3 to 57.2)   | 53.3 (48.2 to 58.3)   |
| Year 5                            | 59.9 (55.1 to 64.5)   | 52.7 (49.7 to 55.7)   | 44.4 (37.1 to 51.9)   | 43.2 (38.2 to 48.3)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 45.5 (36.2 to 55.2)   | 43.8 (38.0 to 49.7)   | 69.0 (62.5 to 74.9)   | 43.6 (33.1 to 54.6)   |
| Year 3                            | 43.6 (34.3 to 53.3)   | 36.5 (31.0 to 42.3)   | 59.0 (52.3 to 65.5)   | 43.6 (33.1 to 54.6)   |
| Year 5                            | 37.6 (28.8 to 47.4)   | 32.1 (26.9 to 37.9)   | 18.6 (13.9 to 24.4)   | 37.2 (27.3 to 48.3)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining an American College of Rheumatology (ACR) Response of ACR70

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining an American College of Rheumatology (ACR) Response of ACR70 |
|-----------------|--|

End point description:

ACR70 Responder Index is a composite of clinical, laboratory, and functional measures in rheumatoid arthritis (RA). An ACR70 Responder is a participant who had  $\geq 70\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 70\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, Health Assessment Questionnaire-Disability Index (HAQ-DI) (assessment of participant's physical function), pain due to RA, and hsCRP. Percentage of participants achieving ACR70 response = (number of ACR70 responders) / (number of participants analyzed) \* 100

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

End point timeframe:

Year 1, 3 and 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 61.3 (56.6 to 65.9)   | 45.7 (42.7 to 48.8)   | 34.9 (28.1 to 42.4)   | 35.8 (31.1 to 40.8)   |
| Year 3                            | 54.4 (49.6 to 59.1)   | 44.1 (41.1 to 47.7)   | 35.5 (27.9 to 37.5)   | 32.5 (27.9 to 37.5)   |
| Year 5                            | 48.2 (43.5 to 53.0)   | 39.1 (36.1 to 42.1)   | 28.4 (22.1 to 35.6)   | 28.4 (24.0 to 33.2)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 28.7 (20.8 to 38.2)   | 25.9 (21.1 to 31.4)   | 42.9 (36.4 to 49.6)   | 26.9 (18.3 to 37.7)   |
| Year 3                            | 24.8 (17.4 to 34.0)   | 21.5 (17.1 to 26.8)   | 35.2 (29.1 to 41.9)   | 21.8 (14.1 to 32.2)   |
| Year 5                            | 23.8 (16.5 to 32.9)   | 18.2 (14.1 to 23.2)   | 12.9 (9.0 to 18.1)    | 19.2 (12.0 to 29.3)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining a Disease Activity Score (DAS28) High-Sensitivity C-Reactive Protein (hsCRP) $\leq 3.2$

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining a Disease Activity Score (DAS28) High-Sensitivity C-Reactive Protein (hsCRP) $\leq 3.2$ |
|-----------------|--|

End point description:

Disease Activity Score (DAS) modified to include 28 joint count (DAS28) consisted of composite score of following variables: tender joint count-28 (TJC28), swollen joint count-28 (SJC28), CRP (mg/L), and Patient's Global Assessment of Disease Activity using VAS (patient's global VAS).  $DAS28-CRP = 0.56 \times \sqrt{TJC28} + 0.28 \times \sqrt{SJC28} + 0.36 \times \ln(CRP + 1) + 0.014 \times \text{patient's global VAS} + 0.96$ . Scores ranged from 1.0-9.4, where lower scores indicated less disease activity, and remission was  $DAS28-CRP < 2.6$ . A decrease in DAS28-CRP indicated an improvement in participant's condition.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 1, 3 and 5 after entry into JADY



| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 81.9 (77.9 to 85.3)   | 71.9 (69.0 to 74.5)   | 66.3 (58.9 to 73.0)   | 68.6 (63.7 to 73.1)   |
| Year 3                            | 71.8 (67.3 to 75.9)   | 65.5 (62.5 to 68.3)   | 59.2 (51.6 to 66.3)   | 59.3 (54.2 to 64.2)   |
| Year 5                            | 61.1 (56.3 to 65.6)   | 58.9 (55.9 to 61.9)   | 46.7 (39.4 to 54.3)   | 50.0 (44.9 to 55.1)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 50.5 (40.9 to 60.0)   | 51.1 (45.2 to 57.0)   | 72.4 (66.0 to 78.0)   | 59.0 (47.9 to 69.2)   |
| Year 3                            | 47.5 (38.1 to 57.2)   | 41.6 (35.9 to 47.5)   | 61.0 (54.2 to 67.3)   | 60.3 (49.2 to 70.4)   |
| Year 5                            | 44.6 (35.2 to 54.3)   | 34.3 (28.9 to 40.1)   | 21.0 (16.0 to 27.0)   | 53.8 (42.9 to 64.5)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining a Disease Activity Score (DAS28) High-Sensitivity C-Reactive Protein (hsCRP) <2.6

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining a Disease Activity Score (DAS28) High-Sensitivity C-Reactive Protein (hsCRP) <2.6 |
|-----------------|--|

End point description:

DAS28 consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), ESR (millimeters per hour), and Patient's Global Assessment of Disease Activity. DAS28 was calculated using following formula:  $\text{DAS28-ESR} = 0.56 \times \sqrt{\text{TJC28} + 0.28 \times \sqrt{\text{SJC28}} + 0.70 \times \ln(\text{ESR}) + 0.014 \times \text{Patient's Global VAS}}$ . Total scores ranged from 1.0-9.4, where lower scores indicated less disease activity.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 1, 3 and 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 65.6 (61.0 to 70.0)   | 52.3 (49.3 to 55.4)   | 50.9 (43.4 to 58.3)   | 46.2 (41.1 to 51.3)   |
| Year 3                            | 59.9 (55.1 to 64.5)   | 51.0 (47.9 to 54.0)   | 43.8 (36.5 to 51.3)   | 43.2 (38.2 to 48.3)   |
| Year 5                            | 51.1 (46.3 to 55.8)   | 44.0 (41.0 to 47.0)   | 36.1 (29.2 to 43.6)   | 37.7 (32.9 to 42.8)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 34.7 (26.1 to 44.3)   | 32.8 (27.6 to 38.6)   | 52.4 (45.6 to 59.0)   | 44.9 (34.3 to 55.9)   |
| Year 3                            | 31.7 (23.4 to 41.3)   | 26.3 (21.4 to 31.8)   | 38.6 (32.2 to 45.3)   | 35.9 (26.1 to 47.0)   |
| Year 5                            | 29.7 (21.7 to 39.2)   | 26.6 (21.8 to 32.2)   | 13.3 (9.4 to 18.6)    | 43.6 (33.1 to 54.6)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Boolean Remission Response

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Maintaining American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) Boolean Remission Response |
|-----------------|---|

End point description:

Boolean-based definition of remission, all 4 criteria below must be met: tender joint count (TJC28)  $\leq 1$ , swollen joint count (SJC28)  $\leq 1$ , hsCRP  $\leq 1$  milligram per deciliter (mg/dL), Patient Global Assessment of Disease Activity using visual analog scale (VAS)  $\leq 1$  cm.

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

End point timeframe:

Year 1, 3, and 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 30.5 (26.3 to 35.1)   | 20.8 (18.4 to 23.4)   | 17.8 (12.7 to 24.2)   | 17.8 (14.2 to 22.0)   |
| Year 3                            | 30.8 (26.6 to 35.4)   | 20.3 (18.0 to 22.9)   | 16.6 (11.7 to 22.9)   | 15.0 (11.7 to 19.1)   |
| Year 5                            | 26.5 (22.5 to 30.9)   | 17.7 (15.5 to 20.1)   | 13.6 (9.2 to 19.6)    | 14.2 (11.0 to 18.2)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 8.9 (4.8 to 16.1)     | 9.5 (6.6 to 13.5)     | 17.1 (12.6 to 22.8)   | 12.8 (7.1 to 22.0)    |
| Year 3                            | 9.9 (5.5 to 17.3)     | 8.0 (5.4 to 11.9)     | 11.9 (8.2 to 17.0)    | 15.4 (9.0 to 25.0)    |
| Year 5                            | 6.9 (3.4 to 13.6)     | 7.3 (4.8 to 11.0)     | 5.2 (2.9 to 9.1)      | 15.4 (9.0 to 25.0)    |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline of Originating Study in Modified Total Sharp Score (mTSS)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline of Originating Study in Modified Total Sharp Score (mTSS) |
|-----------------|--|

End point description:

X-rays of the hands/wrists and feet were scored for structural progression as measured using the mTSS. This methodology quantified the extent of bone erosions and joint space narrowing (JSN) for 44 and 42 joints, with higher scores representing greater damage. The mTSS at a time point is the sum of the erosion (range from 0 to 280) and JSN (range from 0 to 168) scores, for a maximum score of 448. Least Squares Mean (LSM) was calculated using a mixed model for repeated measures (MMRM) with treatment, visit, treatment-by-visit-interactions as fixed categorical effects and baseline and baseline-by-visit-interactions as fixed continuous effects.

APD: All enrolled participants who received at least 1 dose of study drug in JADY with available baseline (from originating study) and at least 1 postbaseline x-ray assessment (collected in JADY) and Year 1 data. Year 1 data not available, 0 participants analyzed. JADW and JADA, 0 participants analyzed due to no data collected in this study

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

End point timeframe:

Baseline, Year 1, Baseline, Year 3; Baseline, Year 5

N represents treatments arms consecutively which corresponds with listings in the header.

| End point values                                       | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                     | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                            | 387 <sup>[2]</sup>    | 870 <sup>[3]</sup>    | 137 <sup>[4]</sup>    | 301 <sup>[5]</sup>    |
| Units: Score on a scale                                |                       |                       |                       |                       |
| least squares mean (confidence interval 95%)           |                       |                       |                       |                       |
| Year 1: N=0, N=0, N=0, N=0, N=0, N=0, N=0, N=0         | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   |
| Year 3: N=387, N=943, N=137, N=301, N=0, N=0, N=0, N=0 | 1.03 (0.94 to 1.67)   | 1.64 (1.38 to 1.90)   | 1.13 (0.61 to 1.66)   | 1.13 (0.78 to 1.48)   |
| Year 5: N=349, N=870, N=127, N=276, N=0, N=0, N=0, N=0 | 1.64 (1.18 to 2.09)   | 2.18 (1.85 to 2.51)   | 1.32 (0.69 to 1.96)   | 1.58 (1.15 to 2.02)   |

Notes:

[2] - 9999=Data not available, zero participants analyzed.

[3] - 9999=Data not available, zero participants analyzed.

[4] - 9999=Data not available, zero participants analyzed.

[5] - 9999=Data not available, zero participants analyzed.

| End point values                                       | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                     | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                            | 0 <sup>[6]</sup>      | 0 <sup>[7]</sup>      | 203 <sup>[8]</sup>    | 0 <sup>[9]</sup>      |
| Units: Score on a scale                                |                       |                       |                       |                       |
| least squares mean (confidence interval 95%)           |                       |                       |                       |                       |
| Year 1: N=0, N=0, N=0, N=0, N=0, N=0, N=0, N=0         | ( to )                | ( to )                | 9999 (9999 to 9999)   | ( to )                |
| Year 3: N=387, N=943, N=137, N=301, N=0, N=0, N=0, N=0 | ( to )                | ( to )                | 1.20 (0.61 to 1.80)   | ( to )                |
| Year 5: N=349, N=870, N=127, N=276, N=0, N=0, N=0, N=0 | ( to )                | ( to )                | 9999 (9999 to 9999)   | ( to )                |

Notes:

[6] - Zero participants analyzed due to no data collected in this study or originating study.

[7] - Zero participants analyzed due to no data collected in this study or originating study.

[8] - 9999 = Data not available, zero participants analyzed.

[9] - Zero participants analyzed due to no data collected in this study or originating study.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With mTSS Change ≤0

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants With mTSS Change ≤0 |
|-----------------|--|

End point description:

X-rays of the hands/wrists and feet were scored for structural progression as measured using the mTSS. This methodology quantified the extent of bone erosions and joint space narrowing (JSN) for 44 and 42 joints, with higher scores representing greater damage. The mTSS at a time point is the sum of the erosion (range from 0 to 280) and JSN (range from 0 to 168) scores, for a maximum score of 448, with higher scores representing greater damage.

APD: All enrolled participants who received at least one dose of study drug. and completed at least 48 weeks in study JADY. Year 1 data not available, zero participants analyzed due to no data collected in this study or originating study.

|  |           |
|--|-----------|
| End point type                         | Secondary |
| End point timeframe:                   |           |
| Year 1, 3, and 5 after entry into JADY |           |

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419 <sup>[10]</sup>   | 1034 <sup>[11]</sup>  | 169 <sup>[12]</sup>   | 366 <sup>[13]</sup>   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   |
| Year 3                            | 53.5 (48.7 to 58.2)   | 53.0 (50.0 to 56.0)   | 0.6 (0.1 to 3.3)      | 0.8 (0.3 to 2.4)      |
| Year 5                            | 1.7 (0.8 to 3.4)      | 0.6 (0.3 to 1.3)      | 0.0 (0.0 to 2.2)      | 0.5 (0.1 to 2.0)      |

Notes:

[10] - 9999 = Data not available, zero participants analyzed

[11] - 9999 = Data not available, zero participants analyzed

[12] - 9999 = Data not available, zero participants analyzed

[13] - 9999 = Data not available, zero participants analyzed

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 0 <sup>[14]</sup>     | 0 <sup>[15]</sup>     | 210 <sup>[16]</sup>   | 0 <sup>[17]</sup>     |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | ( to )                | ( to )                | 9999 (9999 to 9999)   | ( to )                |
| Year 3                            | ( to )                | ( to )                | 0.0 (0.0 to 1.8)      | ( to )                |
| Year 5                            | ( to )                | ( to )                | 0.0 (0.0 to 1.8)      | ( to )                |

Notes:

[14] - No data collected; zero participants analyzed.

[15] - No data collected; zero participants analyzed.

[16] - 9999 = Data not available, zero participants analyzed

[17] - No data collected; zero participants analyzed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline of Originating Study in Joint Space Narrowing

|                 |  |
|-----------------|--|
| End point title | Change From Baseline of Originating Study in Joint Space Narrowing |
|-----------------|--|

End point description:

X-rays of the hands/wrists and feet were assessed for joint space narrowing (JSN) and bone erosions. Assessment of JSN for each hand (15 joints per hand) and foot (6 joints per foot), including subluxation, is scored from 0 to 4, with 0 indicating no (normal) JSN and 4 indicating complete loss of joint space, bony ankylosis or luxation. JSN scores ranged from 0-168. A score of 0 would indicate no change and higher scores represent a worsening of joint space narrowing.

APD: All enrolled participants treated with at least 1 dose of study drug in JADY with available baseline

(from originating study) and at least 1 postbaseline x-ray assessment (collected in JADY). JADW and JADA, zero participants analyzed due to no data collected in this study or originating study.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Baseline, Year 3; Baseline, Year 5  |           |
| N represents treatments arms consecutively which corresponds with listings in the header. |           |

| End point values                                       | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                     | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                            | 387 <sup>[18]</sup>   | 943 <sup>[19]</sup>   | 137 <sup>[20]</sup>   | 301 <sup>[21]</sup>   |
| Units: Score on a scale                                |                       |                       |                       |                       |
| least squares mean (confidence interval 95%)           |                       |                       |                       |                       |
| Year 1: N=0, N=0, N=0, N=0, N=0, N=0, N=0, N=0         | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   |
| Year 3: N=387, N=943, N=137, N=301, N=0, N=0           | 0.45 (0.26 to 0.63)   | 0.72 (0.59 to 0.86)   | 0.54 (0.25 to 0.83)   | 0.44 (0.24 to 0.63)   |
| Year 5: N=349, N=870, N=127, N=276, N=0, N=0, N=0, N=0 | 0.59 (0.36 to 0.83)   | 1.00 (0.84 to 1.17)   | 0.68 (0.34 to 1.02)   | 0.60 (0.37 to 0.83)   |

Notes:

[18] - No data collected; zero participants analyzed.

[19] - No data collected; zero participants analyzed.

[20] - No data collected; zero participants analyzed.

[21] - No data collected; zero participants analyzed.

| End point values                                       | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                     | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                            | 0 <sup>[22]</sup>     | 0 <sup>[23]</sup>     | 203 <sup>[24]</sup>   | 0 <sup>[25]</sup>     |
| Units: Score on a scale                                |                       |                       |                       |                       |
| least squares mean (confidence interval 95%)           |                       |                       |                       |                       |
| Year 1: N=0, N=0, N=0, N=0, N=0, N=0, N=0, N=0         | ( to )                | ( to )                | 9999 (9999 to 9999)   | ( to )                |
| Year 3: N=387, N=943, N=137, N=301, N=0, N=0           | ( to )                | ( to )                | 0.52 (0.23 to 0.82)   | ( to )                |
| Year 5: N=349, N=870, N=127, N=276, N=0, N=0, N=0, N=0 | ( to )                | ( to )                | 9999 (9999 to 9999)   | ( to )                |

Notes:

[22] - No data collected; zero participants analyzed.

[23] - No data collected; zero participants analyzed.

[24] - JAGS, JADW, and JADA: no data collected in this study or originating study, 0 participants analyzed.

[25] - No data collected; zero participants analyzed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline of Originating Study in Duration of Morning Stiffness

|                 |  |
|-----------------|--|
| End point title | Change From Baseline of Originating Study in Duration of Morning Stiffness |
|-----------------|--|

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**End point description:**

Participants reported the duration of their morning joint stiffness (MJS) in hours and minutes. The participants were asked about their duration of morning joint stiffness on the day prior to the study visit to capture actual symptoms, since the participant may have had an atypical morning routine on the day of the study visit. If morning joint stiffness duration was longer than 12 hours (720 minutes), it was truncated to 720 minutes for statistical presentations and analyses. A decrease in duration of morning joint stiffness indicated an improvement in the participant's condition.

APD: All enrolled participants who received at least one dose of study drug in JADY and had evaluable morning stiffness data. There were no baseline data for JADX

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

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**End point timeframe:**

Baseline, Year1 ; Baseline, Year 3; Baseline, Year 5

N represents treatments arms consecutively which corresponds with listings in the header.

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| End point values                               | JADZ 4 mg<br>Baricitinib | JADV 4 mg<br>Baricitinib | JADX 2 mg<br>Baricitinib | JADX 4 mg<br>Baricitinib |
|--|--------------------------|--------------------------|--------------------------|--------------------------|
| Subject group type                             | Reporting group          | Reporting group          | Reporting group          | Reporting group          |
| Number of subjects analysed                    | 450                      | 633                      | 0 <sup>[26]</sup>        | 0 <sup>[27]</sup>        |
| Units: Minutes                                 |                          |                          |                          |                          |
| arithmetic mean (standard deviation)           |                          |                          |                          |                          |
| Yr 1:N=450,N-633,N=0,N=0,N=110,N=308,N=221,N=  | -102.72 (± 155.27)       | -73.53 (± 144.22)        | ()                       | ()                       |
| Yr 3:N=387,N=556,N=0,N=0,N=81,N=222            | -112.41 (± 159.78)       | -77.78 (± 141.01)        | ()                       | ()                       |
| Yr 5:N=330,N=470,N=0,N=0,N=70,N-169,N=128,N=57 | -111.45 (± 164.74)       | -82.48 (± 137.23)        | ()                       | ()                       |

Notes:

[26] - No data collected; zero participants analyzed.

[27] - No data collected; zero participants analyzed.

| End point values                               | JADW 2 mg<br>Baricitinib | JADW 4 mg<br>Baricitinib | JAGS 4 mg<br>Baricitinib | JADA 4 mg<br>Baricitinib |
|--|--------------------------|--------------------------|--------------------------|--------------------------|
| Subject group type                             | Reporting group          | Reporting group          | Reporting group          | Reporting group          |
| Number of subjects analysed                    | 110                      | 308                      | 221                      | 78                       |
| Units: Minutes                                 |                          |                          |                          |                          |
| arithmetic mean (standard deviation)           |                          |                          |                          |                          |
| Yr 1:N=450,N-633,N=0,N=0,N=110,N=308,N=221,N=  | -75.07 (± 139.00)        | 73.88 (± 149.55)         | -68.74 (± 148.34)        | -37.12 (± 61.34)         |
| Yr 3:N=387,N=556,N=0,N=0,N=81,N=222            | -84.60 (± 127.80)        | -67.79 (± 154.05)        | -90.61 (± 147.70)        | -47.13 (± 52.97)         |
| Yr 5:N=330,N=470,N=0,N=0,N=70,N-169,N=128,N=57 | 88.37 (± 146.73)         | -91.57 (± 163.88)        | -92.75 (± 125.39)        | -45.89 (± 60.43)         |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Change From Baseline of Originating Study in European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) Health State Scores (UK)**

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|  |  |
|--|--|
| End point title  | Change From Baseline of Originating Study in European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) Health State Scores (UK) |
| End point description:   |  |
| <p>The European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) is a standardized measure of health status of the participant. The first component is a descriptive system of the respondent's health comprised of the following 5 participant-reported dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The responses are used to derive the health state index scores using the United Kingdom (UK) algorithm, with scores ranging from -0.594 to 1, and the United States (US) algorithm, with scores ranging from -0.109 to 1. A higher score indicates better health state.</p> |  |
| <p>APD: All enrolled participants who received at least 1 dose of study drug and had evaluable EQ-5D-5L data. EQ-5D-5L data was not collected during the JADA originating study, zero participants analyzed.</p>   |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline, Year 1; Baseline, Year 3; Baseline, Year 5   |  |

| End point values                                   | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                 | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                        | 450                   | 1088                  | 171                   | 383                   |
| Units: Score on a scale                            |                       |                       |                       |                       |
| arithmetic mean (standard deviation)               |                       |                       |                       |                       |
| Yr1:N=450,N=1088,N=171,N=383,N=108,N=305,N=221,N=0 | 0.28 (± 0.26)         | 0.23 (± 0.24)         | 0.19 (± 0.26)         | 0.20 (± 0.23)         |
| Yr3:N=386,N=952,N=146,N=309,N=80,N=219,N=190,N=0   | 0.33 (± 0.24)         | 0.24 (± 0.25)         | 0.20 (± 0.26)         | 0.21 (± 0.26)         |
| Yr5:N=330,N=820,N=122,N=264,N=70,N=169,N=127,N=0   | 0.35 (± 0.24)         | 0.26 (± 0.26)         | 0.19 (± 0.25)         | 0.20 (± 0.26)         |

| End point values                                   | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                 | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                        | 108                   | 305                   | 221                   | 0 <sup>[28]</sup>     |
| Units: Score on a scale                            |                       |                       |                       |                       |
| arithmetic mean (standard deviation)               |                       |                       |                       |                       |
| Yr1:N=450,N=1088,N=171,N=383,N=108,N=305,N=221,N=0 | 0.21 (± 0.22)         | 0.19 (± 0.24)         | 0.20 (± 0.26)         | ()                    |
| Yr3:N=386,N=952,N=146,N=309,N=80,N=219,N=190,N=0   | 0.21 (± 0.22)         | 0.22 (± 0.25)         | 0.24 (± 0.24)         | ()                    |
| Yr5:N=330,N=820,N=122,N=264,N=70,N=169,N=127,N=0   | 0.21 (± 0.22)         | 0.22 (± 0.30)         | 0.25 (± 0.26)         | ()                    |

Notes:

[28] - Zero participants analyzed; data not collected.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline of Originating Study in European Quality of Life-5



**Dimensions-5 Level (EQ-5D-5L) Health State Scores (US)**

|                 |  |
|-----------------|--|
| End point title | Change From Baseline of Originating Study in European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) Health State Scores (US) |
|-----------------|--|

End point description:

The European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) is a standardized measure of health status of the participant. The first component is a descriptive system of the respondent's health comprised of the following 5 participant-reported dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The responses are used to derive the health state index scores using the United Kingdom (UK) algorithm, with scores ranging from -0.594 to 1, and the United States (US) algorithm, with scores ranging from -0.109 to 1. A higher score indicates better health state.

APD: All enrolled participants who received at least 1 dose of study drug and had evaluable EQ-5D-5L data. EQ-5D-5L data was not collected during the JADA originating study, zero participants analyzed.

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

End point timeframe:

Baseline, Year 1; Baseline Year 3; Baseline, Year 5

N represents treatments arms consecutively which corresponds with listings in the header.

| End point values                                   | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                 | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                        | 450                   | 1088                  | 171                   | 383                   |
| Units: Score on a scale                            |                       |                       |                       |                       |
| arithmetic mean (standard deviation)               |                       |                       |                       |                       |
| Yr1:N=450,N=1088,N=171,N=383,N=108,N=305,N=221,N=0 | 0.19 (± 0.18)         | 0.16 (± 0.17)         | 0.13 (± 0.18)         | 0.14 (± 0.16)         |
| Yr3:N=386,N=952,N=146,N=309,N=80,N=219,N=190,N=0   | 0.23 (± 0.17)         | 0.17 (± 0.17)         | 0.15 (± 0.18)         | 0.15 (± 0.18)         |
| Yr5:N=330,N=820,N=122,N=264,N=70,N=169,N=127,N=0   | 0.24 (± 0.16)         | 0.18 (± 0.18)         | 0.13 (± 0.17)         | 0.14 (± 0.18)         |

| End point values                                   | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                 | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                        | 108                   | 305                   | 221                   | 0 <sup>[29]</sup>     |
| Units: Score on a scale                            |                       |                       |                       |                       |
| arithmetic mean (standard deviation)               |                       |                       |                       |                       |
| Yr1:N=450,N=1088,N=171,N=383,N=108,N=305,N=221,N=0 | 0.14 (± 0.15)         | 0.13 (± 0.16)         | 0.14 (± 0.18)         | ()                    |
| Yr3:N=386,N=952,N=146,N=309,N=80,N=219,N=190,N=0   | 0.14 (± 0.15)         | 0.15 (± 0.17)         | 0.17 (± 0.17)         | ()                    |
| Yr5:N=330,N=820,N=122,N=264,N=70,N=169,N=127,N=0   | 0.15 (± 0.15)         | 0.15 (± 0.20)         | 0.18 (± 0.18)         | ()                    |

Notes:

[29] - Zero participants analyzed; data not collected.

**Statistical analyses**

**Secondary: Percentage of Participants Maintaining a Clinical Disease Activity Index Score (CDAI)  $\leq 10$** 

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Maintaining a Clinical Disease Activity Index Score (CDAI) $\leq 10$ |
|-----------------|---|

## End point description:

The CDAI is a tool for measurement of disease activity in RA that does not require a laboratory component and was scored by the investigative site. It integrates TJC28 (scored 0-28 with higher scores indicating higher disease activity), SJC28 (scored 0-28 with higher scores indicating higher disease activity), Patient's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity), and Physician's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity). The CDAI is calculated by summing the values of the 4 components. CDAI scores range from 0 to 76; lower scores indicated lower disease activity. A negative change from baseline indicates improvement in condition.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

## End point timeframe:

Year 3 and Year 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 81.6 (77.6 to 85.0)   | 75.3 (72.6 to 77.9)   | 68.6 (61.3 to 75.2)   | 69.9 (65.1 to 74.4)   |
| Year 3                            | 73.3 (68.8 to 77.3)   | 67.7 (64.8 to 70.5)   | 60.4 (52.8 to 67.4)   | 60.4 (55.3 to 65.3)   |
| Year 5                            | 61.6 (56.8 to 66.1)   | 61.1 (58.1 to 64.0)   | 51.5 (44.0 to 58.9)   | 54.6 (49.5 to 59.7)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 52.5 (42.8 to 61.9)   | 50.7 (44.8 to 56.6)   | 73.3 (67.0 to 78.9)   | 60.3 (49.2 to 70.4)   |
| Year 3                            | 49.5 (40.0 to 59.1)   | 44.5 (38.8 to 50.4)   | 61.4 (54.7 to 67.8)   | 56.4 (45.4 to 66.9)   |
| Year 5                            | 44.6 (35.2 to 54.3)   | 35.4 (30.0 to 41.2)   | 21.9 (16.8 to 28.0)   | 56.4 (45.4 to 66.9)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Maintaining a Clinical Disease Activity Index Score (CDAI) $\leq 2.8$

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining a Clinical Disease Activity Index Score (CDAI) $\leq 2.8$ |
|-----------------|--|

End point description:

The CDAI is a tool for measurement of disease activity in RA that does not require a laboratory component and was scored by the investigative site. It integrates TJC28 (scored 0-28 with higher scores indicating higher disease activity), SJC28 (scored 0-28 with higher scores indicating higher disease activity), Patient's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity), and Physician's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity). The CDAI is calculated by summing the values of the 4 components. CDAI scores range from 0 to 76; lower scores indicated lower disease activity. A negative change from baseline indicates improvement in condition.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 3 and Year 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 44.9 (40.2 to 49.7)   | 28.3 (25.7 to 31.2)   | 21.9 (16.3 to 28.7)   | 25.1 (21.0 to 29.8)   |
| Year 3                            | 40.1 (35.5 to 44.9)   | 30.0 (27.3 to 32.8)   | 21.9 (16.3 to 28.7)   | 23.5 (19.4 to 28.1)   |
| Year 5                            | 33.9 (29.5 to 38.6)   | 25.0 (22.5 to 27.8)   | 19.5 (14.3 to 26.2)   | 22.4 (18.4 to 27.0)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 16.8 (10.8 to 25.3)   | 13.5 (10.0 to 18.1)   | 22.9 (17.7 to 29.0)   | 14.1 (8.1 to 23.5)    |
| Year 3                            | 22.8 (15.7 to 31.9)   | 15.0 (11.2 to 19.7)   | 18.6 (13.9 to 24.4)   | 20.5 (13.0 to 30.8)   |
| Year 5                            | 15.8 (10.0 to 24.2)   | 12.8 (9.3 to 17.2)    | 8.1 (5.1 to 12.6)     | 19.2 (12.0 to 29.3)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Maintaining a Health Assessment Questionnaire Disability Index (HAQ-DI) Improvement $\geq 0.22$

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining a Health Assessment Questionnaire Disability Index (HAQ-DI) Improvement $\geq 0.22$ |
|-----------------|--|

End point description:

The HAQ-DI questionnaire assesses the participant's self-perception on the degree of difficulty [0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty), and 3 (unable to do)] when dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, and performing other daily activities. Scores for each functional area were averaged to calculate HAQ-DI scores, which ranged from 0 (no disability) to 3 (worst disability). A decrease in HAQ-DI score indicated an improvement in the participant's condition. An improvement of 0.22 or 0.3 points on the HAQ-DI has been identified as a minimal clinically important difference in Rheumatoid Arthritis participants.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 3 and Year 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 89.7 (86.5 to 92.3)   | 81.4 (78.9 to 83.7)   | 78.7 (71.9 to 84.2)   | 75.4 (70.7 to 79.5)   |
| Year 3                            | 75.4 (71.1 to 79.3)   | 70.4 (67.6 to 73.1)   | 64.5 (57.0 to 71.3)   | 63.4 (58.3 to 68.2)   |
| Year 5                            | 65.2 (60.5 to 69.6)   | 58.5 (55.5 to 61.5)   | 51.5 (44.0 to 58.9)   | 51.4 (46.3 to 56.4)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 74.3 (65.0 to 81.8)   | 69.3 (63.6 to 74.5)   | 80.0 (74.1 to 84.8)   | 48.7 (37.9 to 59.6)   |
| Year 3                            | 56.4 (46.7 to 65.7)   | 54.4 (48.5 to 60.2)   | 68.1 (61.5 to 74.0)   | 47.4 (36.7 to 58.4)   |
| Year 5                            | 50.5 (40.9 to 60.0)   | 39.4 (33.8 to 45.3)   | 20.0 (15.2 to 25.9)   | 39.7 (29.6 to 50.8)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Maintaining a Health Assessment Questionnaire Disability Index (HAQ-DI) Improvement $\geq 0.3$

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Maintaining a Health Assessment Questionnaire Disability Index (HAQ-DI) Improvement $\geq 0.3$ |
|-----------------|---|

End point description:

The HAQ-DI questionnaire assesses the participant's self-perception on the degree of difficulty [0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty), and 3 (unable to do)] when dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, and performing other daily activities. Scores for each functional area were averaged to calculate HAQ-DI scores, which ranged from 0 (no disability) to 3 (worst disability). A decrease in HAQ-DI score indicated an improvement in the participant's condition.

An improvement of 0.22 or 0.3 points on the HAQ-DI has been identified as a minimal clinically important difference in Rheumatoid Arthritis participants.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 3 and Year 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 85.4 (81.7 to 88.5)   | 75.6 (72.9 to 78.1)   | 72.8 (65.6 to 78.9)   | 69.4 (64.5 to 73.9)   |
| Year 3                            | 72.6 (68.1 to 76.6)   | 64.8 (61.8 to 67.6)   | 61.5 (54.0 to 68.5)   | 58.5 (53.4 to 63.4)   |
| Year 5                            | 62.8 (58.0 to 67.3)   | 53.4 (50.3 to 56.4)   | 46.7 (39.4 to 54.3)   | 46.2 (41.1 to 51.3)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 65.3 (55.7 to 73.9)   | 61.7 (55.8 to 67.2)   | 75.2 (69.0 to 80.6)   | 43.6 (33.1 to 54.6)   |
| Year 3                            | 50.5 (40.9 to 60.0)   | 47.8 (42.0 to 53.7)   | 63.8 (57.1 to 70.0)   | 38.5 (28.4 to 49.6)   |
| Year 5                            | 46.5 (37.1 to 56.2)   | 35.0 (29.6 to 40.9)   | 19.5 (14.7 to 25.4)   | 34.6 (25.0 to 45.7)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline of Originating Study in Bone Erosion Score

|                 |   |
|-----------------|---|
| End point title | Change From Baseline of Originating Study in Bone Erosion Score |
|-----------------|---|

End point description:

The joint erosion score is a summary of erosion severity in 32 joints of the hands and 12 joints of the feet. The maximum erosion score for a hand joint is 5 and for a foot joint is 10. Thus, the maximal erosion score is 280 for a timepoint (160 for both hands/ wrists and 120 for both feet). Each joint is scored according to the surface area involved from 0 to 5 for hand joints and 0 to 10 for the foot joints. The highest score (5 for the hand and 10 for the foot) indicates extensive loss of bone from more than one half of the articulating bone. A score of 0 in either the hand or foot joints indicates no erosion.

LSM was calculated using an MMRM model with treatment, baseline value, visit, and the interactions of baseline-by-visit and treatment-by-visit as fixed factors.

APD: All enrolled participants treated with at least 1 dose of study drug in JADY with available baseline (from originating study) and at least 1 postbaseline x-ray assessment (collected in JADY).

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

End point timeframe:

Baseline, Year 1; Baseline, Year 3; Baseline, Year 5 N represents treatments arms consecutively which corresponds with listings in the header.

APD: JADW and JADA, zero participants analyzed due to no data collected in this study or originating study.

| End point values                                       | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                     | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                            | 387 <sup>[30]</sup>   | 943 <sup>[31]</sup>   | 137 <sup>[32]</sup>   | 301 <sup>[33]</sup>   |
| Units: Score on a scale                                |                       |                       |                       |                       |
| least squares mean (confidence interval 95%)           |                       |                       |                       |                       |
| Year 1: N=0, N=0, N=0, N=0, N=0, N=0, N=0, N=0         | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   | 9999 (9999 to 9999)   |
| Year 3: N=387, N=943, N=137, N=301, N=0, N=0, N=0, N=0 | 0.85 (0.63 to 1.08)   | 0.92 (0.76 to 1.07)   | 0.59 (0.30 to 0.89)   | 0.69 (0.49 to 0.89)   |
| Year 5: N=349, N=870, N=127, N=276, N=0, N=0, N=0, N=0 | 1.04 (0.77 to 1.32)   | 1.18 (0.98 to 1.38)   | 0.65 (0.28 to 1.01)   | 0.98 (0.74 to 1.23)   |

Notes:

[30] - 9999 = Data not available, zero participants analyzed.

[31] - 9999 = Data not available, zero participants analyzed.

[32] - 9999 = Data not available, zero participants analyzed.

[33] - 9999 = Data not available, zero participants analyzed.

| End point values | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|------------------|-----------------------|-----------------------|-----------------------|-----------------------|
|------------------|-----------------------|-----------------------|-----------------------|-----------------------|

| Subject group type                                     | Reporting group   | Reporting group   | Reporting group     | Reporting group   |
|--|-------------------|-------------------|---------------------|-------------------|
| Number of subjects analysed                            | 0 <sup>[34]</sup> | 0 <sup>[35]</sup> | 203 <sup>[36]</sup> | 0 <sup>[37]</sup> |
| Units: Score on a scale                                |                   |                   |                     |                   |
| least squares mean (confidence interval 95%)           |                   |                   |                     |                   |
| Year 1: N=0, N=0, N=0, N=0, N=0, N=0, N=0, N=0         | ( to )            | ( to )            | 9999 (9999 to 9999) | ( to )            |
| Year 3: N=387, N=943, N=137, N=301, N=0, N=0, N=0, N=0 | ( to )            | ( to )            | 0.68 (0.32 to 1.03) | ( to )            |
| Year 5: N=349, N=870, N=127, N=276, N=0, N=0, N=0, N=0 | ( to )            | ( to )            | 9999 (9999 to 9999) | ( to )            |

Notes:

[34] - No data collected; zero participants analyzed.

[35] - No data collected; zero participants analyzed.

[36] - 9999 = Data not available, zero participants analyzed.

[37] - No data collected; zero participants analyzed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Healthcare Resource Utilization

|                 |                                 |
|-----------------|---------------------------------|
| End point title | Healthcare Resource Utilization |
|-----------------|---------------------------------|

End point description:

Healthcare resource utilization data will be collected by site staff regarding the number of visits to medical care providers such as general practitioners, specialists, physical or occupational therapists, and other nonphysical care providers for services outside of the clinical study; emergency room admissions; hospital admissions; and concomitant medications related to the treatment of Rheumatoid Arthritis (RA).

APD: All enrolled participants who received at least one dose of study drug, with access healthcare services outside of the clinical study.

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

End point timeframe:

Baseline Up to 84 months

| End point values             | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type           | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed  | 451                   | 1090                  | 180                   | 403                   |
| Units: Consultations         |                       |                       |                       |                       |
| number (not applicable)      |                       |                       |                       |                       |
| Healthcare Consultations     | 3134                  | 11108                 | 2160                  | 4573                  |
| Emergency Room Consultations | 95                    | 244                   | 52                    | 131                   |

| End point values            | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type          | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed | 117                   | 331                   | 221                   | 83                    |
| Units: Consultations        |                       |                       |                       |                       |
| number (not applicable)     |                       |                       |                       |                       |

|                              |      |      |     |     |
|------------------------------|------|------|-----|-----|
| Healthcare Consultations     | 2380 | 5410 | 717 | 749 |
| Emergency Room Consultations | 73   | 154  | 40  | 16  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining a Simplified Disease Activity Index (SDAI) ≤11

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Maintaining a Simplified Disease Activity Index (SDAI) ≤11 |
|-----------------|---|

End point description:

SDAI is a tool for measurement of disease activity in RA that integrates TJC28, SJC28, acute phase response using C-reactive protein (milligrams per liter), Patient's Global Assessment of Disease Activity using VAS centimeters (cm), and Physician's Global Assessment of Disease Activity using VAS (cm). The SDAI is calculated by summing the values of the 5 components. Lower scores indicated less disease activity. The SDAI is expressed as a score on a scale with the minimum score=0 (best) to maximum score=86 (worst). Low disease activity is defined as a SDAI score ≤11.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 1, Year 3, and Year 5 after entry in to JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 81.6 (77.6 to 85.0)   | 75.2 (72.5 to 77.8)   | 70.4 (63.1 to 76.8)   | 69.1 (64.2 to 73.6)   |
| Year 3                            | 73.3 (68.8 to 77.3)   | 67.8 (64.9 to 70.6)   | 60.9 (53.4 to 68.0)   | 62.3 (57.2 to 67.1)   |
| Year 5                            | 61.3 (56.6 to 65.9)   | 61.2 (58.2 to 64.1)   | 51.5 (44.0 to 58.9)   | 53.3 (48.2 to 58.3)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 53.5 (43.8 to 62.9)   | 53.6 (47.7 to 59.5)   | 72.4 (66.0 to 78.0)   | 59.0 (47.9 to 69.2)   |
| Year 3                            | 48.5 (39.0 to 58.1)   | 44.5 (38.8 to 50.4)   | 60.0 (53.3 to 66.4)   | 57.7 (46.6 to 68.0)   |



|        |                     |                     |                     |                     |
|--------|---------------------|---------------------|---------------------|---------------------|
| Year 5 | 46.5 (37.1 to 56.2) | 35.4 (30.0 to 41.2) | 23.3 (18.1 to 29.5) | 57.7 (46.6 to 68.0) |
|--------|---------------------|---------------------|---------------------|---------------------|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining a Simplified Disease Activity Index (SDAI) $\leq 3.3$

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining a Simplified Disease Activity Index (SDAI) $\leq 3.3$ |
|-----------------|--|

End point description:

SDAI is a tool for measurement of disease activity in RA that integrates TJC28, SJC28, acute phase response using C-reactive protein (milligrams per liter), Patient's Global Assessment of Disease Activity using VAS centimeters (cm), and Physician's Global Assessment of Disease Activity using VAS (cm). The SDAI is calculated by summing the values of the 5 components. Lower scores indicated less disease activity. The SDAI is expressed as a score on a scale with the minimum score=0 (best) to maximum score=86 (worst). Disease remission is defined as an SDAI score of  $\leq 3.3$ .

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 1, Year 3 and Year 5

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 45.3 (40.6 to 50.1)   | 28.9 (26.2 to 31.8)   | 24.3 (18.4 to 31.2)   | 23.5 (19.4 to 28.1)   |
| Year 3                            | 39.9 (35.3 to 44.6)   | 29.8 (27.1 to 32.6)   | 22.5 (16.8 to 29.4)   | 21.6 (17.7 to 26.1)   |
| Year 5                            | 34.8 (30.4 to 39.5)   | 24.7 (22.1 to 27.4)   | 20.7 (15.3 to 27.4)   | 21.3 (17.4 to 25.8)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 13.9 (8.4 to 21.9)    | 13.1 (9.6 to 17.7)    | 22.9 (17.7 to 29.0)   | 14.1 (8.1 to 23.5)    |
| Year 3                            | 19.8 (13.2 to 28.6)   | 13.5 (10.0 to 18.1)   | 15.7 (11.4 to 21.2)   | 21.8 (14.1 to 32.2)   |

|        |                    |                    |                   |                     |
|--------|--------------------|--------------------|-------------------|---------------------|
| Year 5 | 13.9 (8.4 to 21.9) | 11.3 (8.1 to 15.6) | 8.1 (5.1 to 12.6) | 21.8 (14.1 to 32.2) |
|--------|--------------------|--------------------|-------------------|---------------------|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with Relapse Event During the 96-Week Step-Down Period

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with Relapse Event During the 96-Week Step-Down Period |
|-----------------|---|

End point description:

Relapse is defined as a Clinical Disease Activity Index score > 10. The CDAI is a tool for measurement of disease activity in RA that does not require a laboratory component and was scored by the investigative site. It integrates TJC28 (scored 0-28 with higher scores indicating higher disease activity), SJC28 (scored 0-28 with higher scores indicating higher disease activity), Patient's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity), and Physician's Global Assessment of Disease Activity (scored on a visual analogue scale from 0-10 cm with higher scores indicating higher disease activity). The CDAI is calculated by summing the values of the 4 components. CDAI scores range from 0 to 76; lower scores indicated lower disease activity. Total number of participants at risk multiplied by estimate of cumulative event probability would need to be rounded up or down to get a whole number.

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

End point timeframe:

Week 0 through Week 96 of Step-down

APD: All enrolled participants who were randomized, were not rescued, and received at least one dose of study drug during the step-down period.

| End point values                  | 2 mg Baricitinib Step-down | 4 mg Baricitinib Step-down |  |  |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type                | Reporting group            | Reporting group            |  |  |
| Number of subjects analysed       | 498                        | 498                        |  |  |
| Units: Percentage of participants |                            |                            |  |  |
| number (not applicable)           |                            |                            |  |  |
| Week 12                           | 11.8                       | 5.4                        |  |  |
| Week 24                           | 26.0                       | 12.5                       |  |  |
| Week 36                           | 31.0                       | 18.2                       |  |  |
| Week 48                           | 36.0                       | 21.1                       |  |  |
| Week 60                           | 41.0                       | 26.6                       |  |  |
| Week 72                           | 45.1                       | 29.1                       |  |  |
| Week 84                           | 46.7                       | 31.0                       |  |  |
| Week 96                           | 47.8                       | 34.5                       |  |  |

## Statistical analyses

## Secondary: Percentage of Participants Maintaining a DAS28-Erythrocyte Sedimentation Rate (ESR) Score of $\leq 3.2$

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Maintaining a DAS28-Erythrocyte Sedimentation Rate (ESR) Score of $\leq 3.2$ |
|-----------------|---|

### End point description:

DAS28 consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), ESR (millimeters per hour), and Patient's Global Assessment of Disease Activity. DAS28 was calculated using following formula:  $\text{DAS28-ESR} = 0.56 \times \sqrt{\text{TJC28}} + 0.28 \times \sqrt{\text{SJC28}} + 0.70 \times \ln(\text{ESR}) + 0.014 \times \text{Patient's Global VAS}$ . Total scores ranged from 1.0-9.4, where lower scores indicated less disease activity.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

### End point timeframe:

Year 1, 3, and 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 61.8 (57.1 to 66.3)   | 48.4 (45.3 to 51.4)   | 46.2 (38.8 to 53.7)   | 48.4 (43.3 to 53.5)   |
| Year 3                            | 54.4 (49.6 to 59.1)   | 46.1 (43.1 to 49.2)   | 40.2 (33.1 to 47.8)   | 41.0 (36.1 to 46.1)   |
| Year 5                            | 48.7 (43.9 to 53.5)   | 41.3 (38.3 to 44.3)   | 36.1 (29.2 to 43.6)   | 32.5 (27.9 to 37.5)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 274                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 31.7 (23.4 to 41.3)   | 31.8 (26.5 to 37.5)   | 41.0 (34.5 to 47.7)   | 35.9 (26.1 to 47.0)   |
| Year 3                            | 22.8 (15.7 to 31.9)   | 23.7 (19.1 to 29.1)   | 33.8 (27.8 to 40.4)   | 37.2 (27.3 to 48.3)   |
| Year 5                            | 23.8 (16.5 to 32.9)   | 21.9 (17.4 to 27.2)   | 11.4 (7.8 to 16.4)    | 37.2 (27.3 to 48.3)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Maintaining a DAS28-Erythrocyte Sedimentation Rate (ESR) Sore of <2.6

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Maintaining a DAS28-Erythrocyte Sedimentation Rate (ESR) Sore of <2.6 |
|-----------------|--|

End point description:

DAS28 consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), ESR (millimeters per hour), and Patient's Global Assessment of Disease Activity. DAS28 was calculated using following formula:  $\text{DAS28-ESR} = 0.56 \times \sqrt{\text{TJC28} + 0.28 \times \sqrt{\text{SJC28}} + 0.70 \times \ln(\text{ESR}) + 0.014 \times \text{Patient's Global VAS}}$ . Total scores ranged from 1.0-9.4, where lower scores indicated less disease activity.

APD: All enrolled participants who received at least one dose of study drug and completed at least 48 weeks in study JADY.

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

End point timeframe:

Year 1, 3, and 5 after entry into JADY

| End point values                  | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 419                   | 1034                  | 169                   | 366                   |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 36.8 (32.3 to 41.5)   | 29.3 (26.6 to 32.2)   | 24.3 (18.4 to 31.2)   | 26.8 (22.5 to 31.5)   |
| Year 3                            | 38.9 (34.4 to 43.7)   | 24.7 (22.1 to 27.4)   | 24.3 (18.4 to 31.2)   | 23.2 (19.2 to 27.8)   |
| Year 5                            | 31.3 (27.0 to 35.9)   | 23.9 (21.4 to 26.6)   | 22.5 (16.8 to 29.4)   | 19.4 (15.7 to 23.8)   |

| End point values                  | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed       | 101                   | 241                   | 210                   | 78                    |
| Units: Percentage of participants |                       |                       |                       |                       |
| number (confidence interval 95%)  |                       |                       |                       |                       |
| Year 1                            | 20.8 (14.0 to 29.7)   | 13.1 (9.6 to 17.7)    | 25.2 (19.8 to 31.5)   | 15.4 (9.0 to 25.0)    |
| Year 3                            | 15.8 (10.0 to 24.2)   | 10.2 (7.2 to 14.4)    | 19.5 (14.7 to 25.4)   | 23.1 (15.1 to 33.6)   |
| Year 5                            | 11.9 (6.9 to 19.6)    | 8.8 (6.0 to 12.7)     | 7.1 (4.4 to 11.4)     | 19.2 (12.0 to 29.3)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline of Originating Study in European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) Scores (Self-Perceived Health)

|  |  |
|--|--|
| End point title  | Change From Baseline of Originating Study in European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) Scores (Self-Perceived Health) |
| End point description:   |  |
| The European Quality of Life-5 Dimensions-5 Level (EQ-5D-5L) is a standardized measure of health status of the participant. The second component is a self-perceived health score which is assessed using a VAS that ranged from 0 to 100 millimeter (mm), where 0 mm indicated the worst health you can imagine and 100 mm indicated the best health you can imagine. |  |
| APD: All enrolled participants who received at least 1 dose of study drug and completed at least 48 weeks in study JADY. EQ-5D-5L data was not collected during the JADA originating study, zero participants analyzed.  |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline, Year 1; Baseline, Year 3; Baseline, Year 5   |  |

| End point values                                   | JADZ 4 mg Baricitinib | JADV 4 mg Baricitinib | JADX 2 mg Baricitinib | JADX 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                 | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                        | 450                   | 1088                  | 171                   | 383                   |
| Units: millimeter(s)                               |                       |                       |                       |                       |
| arithmetic mean (standard deviation)               |                       |                       |                       |                       |
| Yr1:N=450,N=1088,N=171,N=383,N=108,N=305,N=221,N=0 | 24.69 (± 28.50)       | 19.72 (± 28.17)       | 15.13 (± 26.78)       | 18.32 (± 26.35)       |
| Yr3:N=386,N=952,N=146,N=309,N=80,N=219,N=190,N=0   | 28.48 (± 29.88)       | 22.10 (± 28.02)       | 16.29 (± 25.37)       | 16.48 (± 30.24)       |
| Yr5:N=330,N=820,N=122,N=264,N=70,N=169,N=127,N=0   | 31.13 (± 28.15)       | 23.93 (± 28.45)       | 13.82 (± 25.59)       | 19.34 (± 27.48)       |

| End point values                                   | JADW 2 mg Baricitinib | JADW 4 mg Baricitinib | JAGS 4 mg Baricitinib | JADA 4 mg Baricitinib |
|--|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                                 | Reporting group       | Reporting group       | Reporting group       | Reporting group       |
| Number of subjects analysed                        | 108                   | 305                   | 221                   | 0 <sup>[38]</sup>     |
| Units: millimeter(s)                               |                       |                       |                       |                       |
| arithmetic mean (standard deviation)               |                       |                       |                       |                       |
| Yr1:N=450,N=1088,N=171,N=383,N=108,N=305,N=221,N=0 | 20.96 (± 24.53)       | 14.98 (± 30.21)       | 18.47 (± 27.31)       | ()                    |
| Yr3:N=386,N=952,N=146,N=309,N=80,N=219,N=190,N=0   | 23.53 (± 24.70)       | 18.79 (± 30.03)       | 21.45 (± 29.64)       | ()                    |
| Yr5:N=330,N=820,N=122,N=264,N=70,N=169,N=127,N=0   | 26.19 (± 27.09)       | 23.57 (± 31.67)       | 27.31 (± 27.19)       | ()                    |

Notes:

[38] - Zero participants analyzed; data not collected.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up to 84 months.

Adverse event reporting additional description:

All enrolled participants who received at least 1 dose of study drug and did not discontinue the study for the reason 'Lost to Follow-up' at the first postbaseline visit in study JADY.

Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 23.1   |

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | 2 mg Baricitinib |
|-----------------------|------------------|

Reporting group description:

2 mg Baricitinib administered orally once daily throughout the 84-month treatment period.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | 4 mg Baricitinib |
|-----------------------|------------------|

Reporting group description:

4 mg Baricitinib administered orally once daily throughout the 84-month treatment period.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | 2 mg Baricitinib Step-Down |
|-----------------------|----------------------------|

Reporting group description:

2 mg Baricitinib administered orally once daily throughout the 96-week step-down period.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | 4 mg Baricitinib Step-Down |
|-----------------------|----------------------------|

Reporting group description:

4 mg Baricitinib administered orally once daily throughout the 96-week step-down period.

| Serious adverse events  | 2 mg Baricitinib   | 4 mg Baricitinib    | 2 mg Baricitinib Step-Down |
|---|--------------------|---------------------|----------------------------|
| Total subjects affected by serious adverse events                   |                    |                     |                            |
| subjects affected / exposed   | 112 / 297 (37.71%) | 517 / 2579 (20.05%) | 164 / 592 (27.70%)         |
| number of deaths (all causes)                                       | 7                  | 43                  | 14                         |
| number of deaths resulting from adverse events                      | 1                  | 11                  | 4                          |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                     |                            |
| adenocarcinoma of colon   |                    |                     |                            |
| alternative dictionary used: MedDRA 23.1                            |                    |                     |                            |
| subjects affected / exposed   | 0 / 297 (0.00%)    | 1 / 2579 (0.04%)    | 0 / 592 (0.00%)            |
| occurrences causally related to treatment / all                     | 0 / 0              | 0 / 1               | 0 / 0                      |
| deaths causally related to treatment / all                          | 0 / 0              | 0 / 0               | 0 / 0                      |
| adenocarcinoma pancreas   |                    |                     |                            |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 1 / 1            | 0 / 0           |
| anaplastic meningioma                              |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| angiolioma   |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| basal cell carcinoma                               |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| benign neoplasm of skin                            |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| benign neoplasm of thyroid gland                   |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| bladder cancer                                     |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| bowen's disease                                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| brain neoplasm                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| breast cancer                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| breast cancer metastatic                        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 2 / 3            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1            | 0 / 0           |
| cervix carcinoma                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[1]</sup>      | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 1 / 440 (0.23%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cervix carcinoma stage 0                        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[2]</sup>      | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |



|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| clear cell renal cell carcinoma<br>alternative dictionary used:<br>MedDRA 23.1                         |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| colon adenoma<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| colon cancer<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| colorectal cancer stage iv<br>alternative dictionary used:<br>MedDRA 23.1                              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| diffuse large b-cell lymphoma<br>alternative dictionary used:<br>MedDRA 23.1                           |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 3 / 4            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| extranodal marginal zone b-cell<br>lymphoma (malt type)<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| fibrous histiocytoma<br>alternative dictionary used:<br>MedDRA 23.1                                    |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gallbladder cancer                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gastric cancer                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gastric neoplasm                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| giant cell tumour of tendon sheath              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| intraductal proliferative breast lesion         |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| invasive ductal breast carcinoma                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 2 / 297 (0.67%) | 4 / 2579 (0.16%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 2 / 2           | 1 / 4            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| large granular lymphocytosis<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 3 / 3            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| laryngeal cancer<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| large intestine fibroma<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| lentigo maligna<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| leukaemia<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| lipoma<br>alternative dictionary used:<br>MedDRA 23.1                       |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 5            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| lung adenocarcinoma stage iv<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| lung adenocarcinoma<br>alternative dictionary used:<br>MedDRA 23.1                     |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all  | 0 / 1           | 0 / 4            | 1 / 2           |
| deaths causally related to treatment / all   | 0 / 1           | 0 / 2            | 0 / 0           |
| lung cancer metastatic<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all  | 0 / 0           | 1 / 1            | 0 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| lung neoplasm<br>alternative dictionary used:<br>MedDRA 23.1                           |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| lung neoplasm malignant<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all  | 0 / 1           | 1 / 3            | 1 / 2           |
| deaths causally related to treatment / all   | 0 / 0           | 1 / 1            | 1 / 2           |
| lung squamous cell carcinoma metastatic<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 1 / 1            | 0 / 0           |
| lymphocytic leukaemia<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| lymphoproliferative disorder<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all                               | 0 / 0           | 0 / 1            | 3 / 3           |
| deaths causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| malignant fibrous histiocytoma<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0           | 2 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| malignant glioma<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| malignant melanoma<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 1           |
| malignant melanoma in situ<br>alternative dictionary used:<br>MedDRA 23.1     |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                               | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| malignant peritoneal neoplasm<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| malignant pleural effusion<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| meningioma<br>alternative dictionary used:<br>MedDRA 23.1                              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| metastases to central nervous<br>system<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| metastases to peritoneum<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| metastatic gastric cancer<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 1            | 0 / 0           |
| mucoepidermoid carcinoma<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                     | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| mueller's mixed tumour<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed <sup>[3]</sup>      | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| neoplasm malignant                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| neuroendocrine carcinoma of the skin            |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| non-hodgkin's lymphoma                          |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| non-small cell lung cancer metastatic           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1            | 0 / 0           |
| nonkeratinising carcinoma of nasopharynx        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0            | 0 / 0           |
| oesophageal squamous cell carcinoma             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| oral neoplasm benign<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| ovarian adenoma<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed <sup>[4]</sup>                                       | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| ovarian cancer<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |
| subjects affected / exposed <sup>[5]</sup>                                       | 1 / 231 (0.43%) | 2 / 2031 (0.10%) | 0 / 440 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 1           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| ovarian cancer stage iv<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed <sup>[6]</sup>                                       | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| ovarian germ cell teratoma benign<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed <sup>[7]</sup>                                       | 1 / 231 (0.43%) | 0 / 2031 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| paget's disease of nipple<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |



|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| pancreatic carcinoma<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 1 / 1           |
| pancreatic carcinoma metastatic<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                    | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| pancreatic carcinoma stage iv<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                    | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 1            | 0 / 0           |
| papillary cystadenoma<br>lymphomatosum<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                    | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| papillary thyroid cancer<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                    | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| prostate cancer<br>alternative dictionary used:<br>MedDRA 23.1                        |                 |                  |                 |
| subjects affected / exposed <sup>[8]</sup>  | 1 / 66 (1.52%)  | 3 / 548 (0.55%)  | 2 / 152 (1.32%) |
| occurrences causally related to<br>treatment / all                                    | 0 / 2           | 1 / 3            | 0 / 2           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| prostate cancer metastatic<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed <sup>[9]</sup>      | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| prostatic adenoma                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[10]</sup>     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| rectal cancer                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| renal cancer                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| renal cell carcinoma                            |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| skin cancer                                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| small cell lung cancer metastatic               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 1 / 1           |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| squamous cell carcinoma<br>alternative dictionary used:<br>MedDRA 23.1                         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| squamous cell carcinoma of lung<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 2 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 1 / 1            | 0 / 0           |
| squamous cell carcinoma of skin<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| squamous cell carcinoma of the<br>cervix<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[11]</sup>  | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| squamous cell carcinoma of the<br>parotid gland<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| t-cell lymphoma<br>alternative dictionary used:<br>MedDRA 23.1                                 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| thyroid cancer stage i<br>alternative dictionary used:<br>MedDRA 23.1                          |                 |                  |                 |

|  |                 |                   |                 |
|--|-----------------|-------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0             | 0 / 0           |
| uterine carcinoma in situ<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                   |                 |
| subjects affected / exposed <sup>[12]</sup>                              | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 440 (0.23%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 0             | 0 / 1           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0             | 0 / 0           |
| uterine cancer<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                   |                 |
| subjects affected / exposed <sup>[13]</sup>                              | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 440 (0.23%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 0             | 0 / 1           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0             | 0 / 0           |
| uterine leiomyoma<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                   |                 |
| subjects affected / exposed <sup>[14]</sup>                              | 0 / 231 (0.00%) | 2 / 2031 (0.10%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 3             | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0             | 0 / 0           |
| Vascular disorders   |                 |                   |                 |
| aortic arteriosclerosis<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                   |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 0             | 0 / 2           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0             | 0 / 0           |
| deep vein thrombosis<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                   |                 |
| subjects affected / exposed  | 4 / 297 (1.35%) | 14 / 2579 (0.54%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all                          | 0 / 4           | 5 / 16            | 2 / 3           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0             | 0 / 0           |
| embolism arterial<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                   |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1            | 0 / 0           |
| essential hypertension                          |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| haematoma                                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 2 / 297 (0.67%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| haemorrhage                                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hypertensive crisis                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hypertension                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hypotension                                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |  |
|--|-----------------|------------------|-----------------|--|
| hypovolaemic shock                                 |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 1           |  |
| intermittent claudication                          |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| jugular vein thrombosis                            |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| necrosis ischaemic                                 |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| peripheral artery stenosis                         |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| peripheral ischaemia                               |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 4            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| peripheral venous disease                          |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| rheumatoid vasculitis                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| thrombophlebitis                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| thrombosed varicose vein                        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| varicose vein                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| vasculitis                                      |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| venous thrombosis                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| venous thrombosis limb<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| Surgical and medical procedures  |                 |                  |                 |
| arthrodesis<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| cataract operation<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| finger amputation<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| hysterectomy<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed <sup>[15]</sup>                                  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 440 (0.23%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| internal fixation of fracture<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| joint arthroplasty<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |



|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| knee arthroplasty<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed  | 2 / 297 (0.67%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 2           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| limb reconstructive surgery<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| rehabilitation therapy<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| scar excision<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| shoulder arthroplasty<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| vaginal cyst excision<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed <sup>[16]</sup>                                | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                                   |                                    |                                   |
|---|-----------------------------------|------------------------------------|-----------------------------------|
| Pregnancy, puerperium and perinatal conditions<br>abortion spontaneous<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[17]</sup><br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 1 / 231 (0.43%)<br>1 / 1<br>0 / 0 | 2 / 2031 (0.10%)<br>2 / 2<br>0 / 0 | 0 / 592 (0.00%)<br>0 / 0<br>0 / 0 |
| pregnancy<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[18]</sup><br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 231 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 2031 (0.05%)<br>0 / 1<br>0 / 0 | 1 / 440 (0.23%)<br>0 / 1<br>0 / 0 |
| General disorders and administration site conditions<br>adverse drug reaction<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all          | 1 / 297 (0.34%)<br>0 / 1<br>0 / 0 | 0 / 2579 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 592 (0.00%)<br>0 / 0<br>0 / 0 |
| alcohol interaction<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 297 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 2579 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 592 (0.17%)<br>0 / 1<br>0 / 0 |
| chest pain<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | 0 / 297 (0.00%)<br>0 / 0<br>0 / 0 | 3 / 2579 (0.12%)<br>0 / 3<br>0 / 0 | 0 / 592 (0.00%)<br>0 / 0<br>0 / 0 |
| complication associated with device<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | 0 / 297 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 2579 (0.04%)<br>0 / 1<br>0 / 0 | 0 / 592 (0.00%)<br>0 / 0<br>0 / 0 |
| death   |                                   |                                    |                                   |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 1           | 0 / 2            | 0 / 0           |
| exercise tolerance decreased                       |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| general physical health deterioration              |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| mucosal inflammation                               |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| multiple organ dysfunction syndrome                |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 1           |
| non-cardiac chest pain                             |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 2 / 297 (0.67%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 2           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| pain   |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| pyrexia   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 2 / 297 (0.67%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 2 / 4           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| sudden cardiac death                            |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1            | 0 / 0           |
| systemic inflammatory response syndrome         |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Immune system disorders                         |                 |                  |                 |
| anaphylactic reaction                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hypersensitivity                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Social circumstances                            |                 |                  |                 |
| respite care                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Reproductive system and breast disorders        |                 |                  |                 |
| adnexa uteri cyst                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[19]</sup>     | 0 / 231 (0.00%) | 2 / 2031 (0.10%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| bartholin's cyst                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[20]</sup>     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 440 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| benign prostatic hyperplasia                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[21]</sup>     | 0 / 66 (0.00%)  | 1 / 548 (0.18%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cervical cyst                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[22]</sup>     | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cervical dysplasia                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[23]</sup>     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 2 / 440 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| dysfunctional uterine bleeding                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed <sup>[24]</sup>                            | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 440 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| endometrial hyperplasia<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed <sup>[25]</sup>                            | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| endometrial hypertrophy<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed <sup>[26]</sup>                            | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 440 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| endometriosis<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed <sup>[27]</sup>                            | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 2 / 440 (0.45%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 1            | 0 / 2           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| genital prolapse<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| metrorrhagia<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed <sup>[28]</sup>                            | 0 / 231 (0.00%) | 4 / 2031 (0.20%) | 0 / 440 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 5            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| ovarian cyst<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed <sup>[29]</sup>                            | 0 / 231 (0.00%) | 3 / 2031 (0.15%) | 0 / 440 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 4            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| pelvic pain<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed                                   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| testicular cyst<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[30]</sup>               | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 152 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| uterine polyp<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[31]</sup>                 | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 440 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| uterine prolapse<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[32]</sup>              | 1 / 231 (0.43%) | 0 / 2031 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| vaginal haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[33]</sup>           | 1 / 231 (0.43%) | 0 / 2031 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| vaginal prolapse<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[34]</sup>              | 0 / 231 (0.00%) | 1 / 2031 (0.05%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| Respiratory, thoracic and mediastinal<br>disorders<br>acute pulmonary oedema<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                    | 1 / 1           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 1 / 1            | 0 / 0           |
| acute respiratory distress syndrome<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| acute respiratory failure<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 5 / 2579 (0.19%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                    | 0 / 0           | 0 / 5            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 1            | 0 / 0           |
| allergic bronchitis<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                    | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| asthma<br>alternative dictionary used:<br>MedDRA 23.1                              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                    | 0 / 0           | 1 / 4            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| atelectasis<br>alternative dictionary used:<br>MedDRA 23.1                         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| bronchitis chronic<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |



|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| bronchopneumopathy<br>alternative dictionary used:<br>MedDRA 23.1                       |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| bronchospasm<br>alternative dictionary used:<br>MedDRA 23.1                             |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                      | 0 / 0           | 1 / 1            | 0 / 2           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| chronic obstructive pulmonary<br>disease<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 9 / 2579 (0.35%) | 2 / 592 (0.34%) |
| occurrences causally related to<br>treatment / all                                      | 3 / 3           | 2 / 17           | 0 / 11          |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 1            | 0 / 0           |
| cough<br>alternative dictionary used:<br>MedDRA 23.1                                    |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                      | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| interstitial lung disease<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 5 / 2579 (0.19%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                      | 0 / 0           | 3 / 6            | 0 / 1           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| lung disorder<br>alternative dictionary used:<br>MedDRA 23.1                            |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                      | 0 / 1           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| nasal polyps<br>alternative dictionary used:<br>MedDRA 23.1                             |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| obstructive airways disorder<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| organising pneumonia<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 2 / 3            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| pleural effusion<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                             | 1 / 1           | 1 / 3            | 0 / 1           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| pleurisy<br>alternative dictionary used:<br>MedDRA 23.1                     |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 0 / 0            | 2 / 2           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| pneumonia aspiration<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                             | 0 / 1           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 1            | 0 / 0           |
| pneumonitis<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                   |                 |
|--|-----------------|-------------------|-----------------|
| pneumothorax<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                   |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                             | 0 / 4           | 0 / 0             | 0 / 0           |
| deaths causally related to<br>treatment / all                                  | 0 / 0           | 0 / 0             | 0 / 0           |
| pulmonary arterial hypertension<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                   |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                             | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to<br>treatment / all                                  | 0 / 0           | 0 / 0             | 0 / 0           |
| pulmonary embolism<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                   |                 |
| subjects affected / exposed  | 5 / 297 (1.68%) | 18 / 2579 (0.70%) | 5 / 592 (0.84%) |
| occurrences causally related to<br>treatment / all                             | 4 / 8           | 6 / 21            | 1 / 5           |
| deaths causally related to<br>treatment / all                                  | 0 / 0           | 1 / 2             | 0 / 2           |
| pulmonary hypertension<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                   |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                             | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to<br>treatment / all                                  | 0 / 0           | 0 / 0             | 0 / 0           |
| pulmonary mass<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                   |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                             | 0 / 0           | 0 / 1             | 1 / 1           |
| deaths causally related to<br>treatment / all                                  | 0 / 0           | 0 / 0             | 0 / 0           |
| pulmonary oedema<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                   |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                             | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to<br>treatment / all                                  | 0 / 0           | 0 / 0             | 0 / 0           |
| respiratory failure<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                   |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 6 / 2579 (0.23%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 1 / 7            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1            | 0 / 0           |
| respiratory arrest                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| sleep apnoea syndrome                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| vocal cord polyp                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Psychiatric disorders                           |                 |                  |                 |
| anxiety   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| confusional state                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| depressed mood                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| depression                                      |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 5            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| mental disorder                                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| mental status changes                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| suicidal ideation                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| suicide attempt                                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Product issues                                  |                 |                  |                 |
| device dislocation                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| device failure                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| device loosening                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Hepatobiliary disorders                         |                 |                  |                 |
| bile duct stone                                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| biliary colic                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| biliary obstruction                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cholangitis                                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cholecystitis                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 2 / 297 (0.67%) | 4 / 2579 (0.16%) | 3 / 592 (0.51%) |
| occurrences causally related to treatment / all | 0 / 2           | 2 / 5            | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cholecystitis chronic                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cholecystitis acute                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 4            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cholelithiasis                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 8 / 2579 (0.31%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 9            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gallbladder polyp                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hepatic cirrhosis                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| liver disorder<br>alternative dictionary used:<br>MedDRA 23.1                            |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| nonalcoholic fatty liver disease<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                       | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| Investigations   |                 |                  |                 |
| blood creatine phosphokinase<br>increased<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 2 / 592 (0.34%) |
| occurrences causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0            | 2 / 2           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| blood glucose increased<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                       | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| blood pressure increased<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| cardiac murmur<br>alternative dictionary used:<br>MedDRA 23.1                            |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                       | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| electrocardiogram t wave inversion<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |



|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| electrocardiogram change<br>alternative dictionary used:<br>MedDRA 23.1                            |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| glomerular filtration rate decreased<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| haemoglobin decreased<br>alternative dictionary used:<br>MedDRA 23.1                               |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| influenza a virus test positive<br>alternative dictionary used:<br>MedDRA 23.1                     |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| mycobacterium tuberculosis complex<br>test positive<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| transaminases increased<br>alternative dictionary used:<br>MedDRA 23.1                             |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |                  |                 |
| accident  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| ankle fracture                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| brain herniation                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1            | 0 / 0           |
| burns second degree                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| carbon monoxide poisoning                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cervical vertebral fracture                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 1 / 1            | 0 / 1           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| colon injury<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| compression fracture<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| contusion<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| crush injury<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| dislocation of vertebra<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| epiphyseal injury<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                   |                 |
|--|-----------------|-------------------|-----------------|
| face injury  |                 |                   |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0             | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| fall   |                 |                   |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                        | 2 / 297 (0.67%) | 13 / 2579 (0.50%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 1 / 2           | 0 / 14            | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| femoral neck fracture                              |                 |                   |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 1 / 2579 (0.04%)  | 2 / 592 (0.34%) |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 1             | 0 / 2           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| femur fracture                                     |                 |                   |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 7 / 2579 (0.27%)  | 3 / 592 (0.51%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 8             | 0 / 3           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| fibula fracture                                    |                 |                   |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0             | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| foot fracture                                      |                 |                   |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 3 / 2579 (0.12%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 3             | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| hand fracture                                      |                 |                   |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| head injury                                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hip fracture                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 5 / 2579 (0.19%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 5            | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| humerus fracture                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 4            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| injury  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| joint dislocation                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3            | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| joint injury                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |  |
|--|-----------------|------------------|-----------------|--|
| keratorhexis                                       |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| ligament rupture                                   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 3            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| lower limb fracture                                |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 4            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| lumbar vertebral fracture                          |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 2            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| meniscus injury                                    |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 7 / 2579 (0.27%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 7            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| open globe injury                                  |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| open fracture                                      |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| overdose  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| patella fracture                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| pelvic fracture                                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| periprosthetic fracture                         |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| post procedural haematoma                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| post procedural complication                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| post procedural haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| radius fracture<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| rib fracture<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| road traffic accident<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| scapula fracture<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| seroma<br>alternative dictionary used:<br>MedDRA 23.1                      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| skin wound<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |



|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| skull fracture                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| spinal compression fracture                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 6 / 2579 (0.23%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 6            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| suture rupture                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| synovial rupture                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| tendon injury                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| tendon rupture                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 5           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| thoracic vertebral fracture<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| tibia fracture<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 3            | 0 / 1           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| toxicity to various agents<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| traumatic arthritis<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| upper limb fracture<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| wound<br>alternative dictionary used:<br>MedDRA 23.1                       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| wound dehiscence<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| wrist fracture                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Congenital, familial and genetic disorders      |                 |                  |                 |
| congenital central nervous system anomaly       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hydrocele                                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed <sup>[35]</sup>     | 0 / 66 (0.00%)  | 1 / 548 (0.18%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hypertrophic cardiomyopathy                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Cardiac disorders                               |                 |                  |                 |
| acute coronary syndrome                         |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| acute left ventricular failure                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| acute myocardial infarction<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 4 / 297 (1.35%) | 7 / 2579 (0.27%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                            | 2 / 5           | 1 / 7            | 1 / 1           |
| deaths causally related to treatment / all                                 | 0 / 1           | 0 / 2            | 0 / 0           |
| angina pectoris<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                            | 0 / 1           | 1 / 3            | 1 / 1           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| angina unstable<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 5 / 2579 (0.19%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                            | 1 / 1           | 2 / 5            | 0 / 1           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| aortic valve disease<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| aortic valve incompetence<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 3           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| aortic valve stenosis<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 4            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                 |                   |                 |
|---|-----------------|-------------------|-----------------|
| arteriosclerosis coronary artery<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 1             | 0 / 2           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0             | 0 / 0           |
| atrial fibrillation<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                   |                 |
| subjects affected / exposed   | 4 / 297 (1.35%) | 11 / 2579 (0.43%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                              | 0 / 5           | 4 / 13            | 0 / 1           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0             | 0 / 0           |
| atrial tachycardia<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0             | 0 / 0           |
| atrioventricular block complete<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 0             | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0             | 0 / 0           |
| bradycardia<br>alternative dictionary used:<br>MedDRA 23.1                      |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 2             | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0             | 0 / 0           |
| bundle branch block left<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 0             | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0             | 0 / 0           |
| cardiac arrest<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                   |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 4            | 0 / 2           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 2            | 0 / 1           |
| cardiac failure<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                 | 0 / 3           | 0 / 1            | 1 / 1           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 1 / 1           |
| cardiac failure acute<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| cardiac failure chronic<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| cardiac failure congestive<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed   | 3 / 297 (1.01%) | 4 / 2579 (0.16%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                 | 1 / 3           | 0 / 4            | 0 / 1           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| cardio-respiratory arrest<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 2            | 0 / 1           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 2            | 0 / 1           |
| chronic left ventricular failure<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |

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| coronary artery disease<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 1           | 0 / 6            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| coronary artery occlusion<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| coronary artery stenosis<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 0 / 0            | 1 / 2           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| mitral valve disease<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| mitral valve incompetence<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| myocardial infarction<br>alternative dictionary used:<br>MedDRA 23.1     |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 2 / 592 (0.34%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 3 / 6            | 1 / 3           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| myocardial ischaemia<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| palpitations                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| pericarditis                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| right ventricular failure                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 1            | 0 / 0           |
| sinus node dysfunction                          |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| sinus tachycardia                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| stress cardiomyopathy                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |



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| supraventricular tachycardia<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                           | 0 / 2           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| ventricular arrhythmia<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| ventricular fibrillation<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| ventricular tachycardia<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                           | 0 / 1           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| Nervous system disorders   |                 |                  |                 |
| amyotrophic lateral sclerosis<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| autonomic neuropathy<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| basal ganglia haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1     |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| central nervous system vasculitis<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebellar infarction<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebellar stroke<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebral artery stenosis<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebral artery thrombosis<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebral haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                       | 0 / 0           | 0 / 0            | 0 / 0           |

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| cerebral infarction<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 1 / 2            | 0 / 1           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebral microhaemorrhage<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebral thrombosis<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebral venous thrombosis<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebrospinal fistula<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebrospinal fluid leakage<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebrovascular accident<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| cerebrovascular disorder<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| cervical cord compression<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| cervical radiculopathy<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| dementia<br>alternative dictionary used:<br>MedDRA 23.1                         |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| depressed level of consciousness<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| dizziness<br>alternative dictionary used:<br>MedDRA 23.1                        |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |

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| embolic stroke                                     |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| epilepsy   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| haemorrhage intracranial                           |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| haemorrhagic stroke                                |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 5 / 2579 (0.19%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 5            | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 1            | 0 / 0           |  |
| headache   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 1            | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| hemiparesis  |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| intercostal neuralgia                              |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| intracranial aneurysm                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| ischaemic cerebral infarction                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| ischaemic stroke                                |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 5 / 297 (1.68%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 7           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0            | 0 / 0           |
| leukoencephalopathy                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| loss of consciousness                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| metabolic encephalopathy                        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|  |                 |                  |                 |  |
|--|-----------------|------------------|-----------------|--|
| migraine   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| myelopathy   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 2 / 3            | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| neuralgia  |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| neuropathy peripheral                              |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| peripheral sensorimotor neuropathy                 |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| post herpetic neuralgia                            |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| presyncope   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| radiculopathy                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| sciatica  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| seizure   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| sensory disturbance                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| subarachnoid haemorrhage                        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| syncope   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 9 / 2579 (0.35%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 10           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |



|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| thalamus haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| transient ischaemic attack<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 1 / 4            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| Blood and lymphatic system disorders                                      |                 |                  |                 |
| anaemia<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |
| subjects affected / exposed   | 2 / 297 (0.67%) | 3 / 2579 (0.12%) | 2 / 592 (0.34%) |
| occurrences causally related to<br>treatment / all                        | 1 / 2           | 3 / 4            | 0 / 2           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| coagulopathy<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 1            | 0 / 0           |
| febrile neutropenia<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| leukocytosis<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| lymphopenia<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| normochromic normocytic anaemia<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| normocytic anaemia<br>alternative dictionary used:<br>MedDRA 23.1                                 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| pancytopenia<br>alternative dictionary used:<br>MedDRA 23.1                                       |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all   | 1 / 1           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| thrombocytopenia<br>alternative dictionary used:<br>MedDRA 23.1                                   |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| thrombocytosis<br>alternative dictionary used:<br>MedDRA 23.1                                     |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all   | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0           | 0 / 0            | 0 / 0           |
| Ear and labyrinth disorders<br>conductive deafness<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| deafness unilateral<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| meniere's disease<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| sudden hearing loss<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| vertigo<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| vertigo positional<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| Eye disorders<br>cataract<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 6 / 2579 (0.23%) | 3 / 592 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 2 / 13           | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cataract subcapsular                            |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| corneal perforation                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| dry age-related macular degeneration            |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| glaucoma  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| keratitis                                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| macular rupture                                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| ocular hypertension                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| retinal detachment                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| rhegmatogenous retinal detachment               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Gastrointestinal disorders                      |                 |                  |                 |
| abdominal pain                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| abdominal pain upper                            |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| abdominal wall haematoma                        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| anal fistula                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| colitis   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 2 / 3            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| colitis ischaemic                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| colitis ulcerative                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| dental cyst                                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| diarrhoea                                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| diverticular perforation<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 1 / 1           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| diverticulum<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| diverticulum intestinal<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| duodenal ulcer haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| duodenitis<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 2            | 0 / 1           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| dysphagia<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| enterocolitis<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |

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|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 0 / 0            | 2 / 2           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| gastric ulcer<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 1 / 3            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| gastric ulcer haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| gastritis<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 2           | 2 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| gastric ulcer perforation<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| gastritis erosive<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 0            | 0 / 0           |
| gastrointestinal haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                             | 1 / 1           | 0 / 3            | 0 / 1           |
| deaths causally related to treatment / all                                  | 0 / 0           | 0 / 1            | 0 / 0           |



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| gastroesophageal reflux disease                    |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| haemorrhoids                                       |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hiatus hernia                                      |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| ileus  |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| inguinal hernia                                    |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| intestinal obstruction                             |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| intestinal perforation                             |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |

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| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| irritable bowel syndrome<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| obstructive pancreatitis<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| oesophageal stenosis<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| pancreatitis acute<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 6 / 2579 (0.23%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 1 / 7            | 0 / 1           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| parotid gland enlargement<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| rectal haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |

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| rectal polyp                                       |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| reflux gastritis                                   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| small intestinal obstruction                       |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 5            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| upper gastrointestinal haemorrhage                 |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 1 / 1           | 1 / 2            | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| umbilical hernia                                   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| volvulus   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |  |
| vomiting   |                 |                  |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                 |                  |                 |
| actinic keratosis                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| angioedema                                      |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| diabetic ulcer                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| eczema asteatotic                               |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| granuloma skin                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| skin ulcer                                      |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                       | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| skin necrosis<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                       | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| Renal and urinary disorders   |                 |                  |                 |
| acute kidney injury<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                       | 1 / 3           | 0 / 4            | 0 / 0           |
| deaths causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| bladder prolapse<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                       | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| calculus bladder<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                       | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| calculus urinary<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                       | 0 / 0           | 0 / 0            | 0 / 2           |
| deaths causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| chronic kidney disease<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 1            | 0 / 0           |
| glomerulonephritis membranous<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| hydronephrosis<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 3            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| iga nephropathy<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| nephrolithiasis<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed  | 2 / 297 (0.67%) | 5 / 2579 (0.19%) | 3 / 592 (0.51%) |
| occurrences causally related to treatment / all                              | 0 / 2           | 0 / 5            | 0 / 3           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| oliguria<br>alternative dictionary used:<br>MedDRA 23.1                      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| proteinuria<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 2 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |

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| renal colic<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| renal cyst<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| renal injury<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 3           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| renal pain<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| renal vein thrombosis<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| stress urinary incontinence<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                          | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| tubulointerstitial nephritis<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                           | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| ureterolithiasis<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 6 / 2579 (0.23%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                           | 0 / 0           | 0 / 7            | 0 / 0           |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| urinary tract inflammation<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                           | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| Endocrine disorders   |                 |                  |                 |
| adrenal suppression<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                           | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| goitre<br>alternative dictionary used:<br>MedDRA 23.1                     |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                           | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| hyperparathyroidism<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                           | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| Musculoskeletal and connective tissue disorders                           |                 |                  |                 |
| acquired claw toe<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |



|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| arthralgia                                      |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 2 / 297 (0.67%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| arthritis                                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3            | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| back pain                                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 5 / 2579 (0.19%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 8            | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| cervical spinal stenosis                        |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| chondrocalcinosis pyrophosphate                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| diastasis recti abdominis                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| foot deformity<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 4 / 2579 (0.16%) | 3 / 592 (0.51%) |
| occurrences causally related to<br>treatment / all                              | 0 / 2           | 0 / 5            | 0 / 6           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| fracture delayed union<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| haematoma muscle<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| intervertebral disc compression<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| intervertebral disc degeneration<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| intervertebral disc disorder<br>alternative dictionary used:<br>MedDRA 23.1     |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                              | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| intervertebral disc protrusion<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |

|   |                 |                   |                 |
|---|-----------------|-------------------|-----------------|
| subjects affected / exposed                     | 1 / 297 (0.34%) | 7 / 2579 (0.27%)  | 5 / 592 (0.84%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 7             | 0 / 7           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| joint destruction                               |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0             | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| lumbar spinal stenosis                          |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 4 / 2579 (0.16%)  | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 5             | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| mixed connective tissue disease                 |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| muscular weakness                               |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| musculoskeletal chest pain                      |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1             | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| osteoarthritis                                  |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 8 / 297 (2.69%) | 42 / 2579 (1.63%) | 6 / 592 (1.01%) |
| occurrences causally related to treatment / all | 0 / 13          | 4 / 56            | 0 / 9           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |

|  |                 |                  |                 |  |
|--|-----------------|------------------|-----------------|--|
| osteochondrosis<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |  |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all                   | 0 / 0           | 0 / 3            | 0 / 0           |  |
| deaths causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |  |
| osteonecrosis<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |  |
| subjects affected / exposed  | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 2 / 592 (0.34%) |  |
| occurrences causally related to<br>treatment / all                   | 0 / 1           | 0 / 2            | 0 / 2           |  |
| deaths causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |  |
| osteoporosis<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |  |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all                   | 0 / 0           | 0 / 0            | 0 / 1           |  |
| deaths causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |  |
| osteoporotic fracture<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |  |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all                   | 0 / 1           | 0 / 0            | 0 / 0           |  |
| deaths causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |  |
| pain in extremity<br>alternative dictionary used:<br>MedDRA 23.1     |                 |                  |                 |  |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all                   | 0 / 0           | 0 / 2            | 0 / 0           |  |
| deaths causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |  |
| rhabdomyolysis<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |  |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all                   | 0 / 0           | 0 / 2            | 0 / 0           |  |
| deaths causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |  |
| rheumatoid arthritis<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |  |

|   |                 |                   |                 |
|---|-----------------|-------------------|-----------------|
| subjects affected / exposed                     | 4 / 297 (1.35%) | 16 / 2579 (0.62%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6           | 1 / 18            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| rheumatoid nodule                               |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| rotator cuff syndrome                           |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| scoliosis                                       |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| spinal osteoarthritis                           |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| spinal instability                              |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| spinal pain                                     |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 2 / 2579 (0.08%)  | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3             | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| spinal stenosis                                    |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 6            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| spondylolisthesis                                  |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| spondyloarthropathy                                |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| synovial cyst                                      |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| synovitis  |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| tendonitis   |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| tenosynovitis                                      |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Infections and infestations                     |                 |                  |                 |
| abdominal infection                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 1            | 0 / 0           |
| abdominal wall abscess                          |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| abscess intestinal                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| abscess limb                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| anal abscess                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| appendicitis perforated                         |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| appendicitis                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 2 / 297 (0.67%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 1 / 3            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1            | 0 / 0           |
| arthritis bacterial                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 2 / 3            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| arthritis infective                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| atypical pneumonia                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 4            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| bacteraemia                                     |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| bacterial infection                             |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |



|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| bone tuberculosis<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 2 / 3            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| breast abscess<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| bronchitis<br>alternative dictionary used:<br>MedDRA 23.1                        |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 5 / 2579 (0.19%) | 2 / 592 (0.34%) |
| occurrences causally related to<br>treatment / all                               | 0 / 1           | 3 / 6            | 3 / 3           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| bronchitis viral<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| bursitis infective<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| bursitis infective staphylococcal<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| covid-19<br>alternative dictionary used:<br>MedDRA 23.1                          |                 |                  |                 |

|   |                 |                   |                 |
|---|-----------------|-------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1             | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1             | 0 / 0           |
| covid-19 pneumonia                              |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| cellulitis                                      |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 3 / 297 (1.01%) | 12 / 2579 (0.47%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3           | 7 / 14            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| cholecystitis infective                         |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0             | 0 / 0           |
| chronic sinusitis                               |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| chronic tonsillitis                             |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |
| coronavirus infection                           |                 |                   |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                   |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2             | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1             | 0 / 0           |

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| cystitis<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 1 / 1           | 2 / 3            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| cytomegalovirus hepatitis<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| cytomegalovirus infection<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| dengue fever<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| device related infection<br>alternative dictionary used:<br>MedDRA 23.1  |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 1           | 2 / 5            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| device related sepsis<br>alternative dictionary used:<br>MedDRA 23.1     |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                       | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| disseminated tuberculosis<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 3 / 3            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 1            | 0 / 0           |
| diverticulitis                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 3 / 297 (1.01%) | 4 / 2579 (0.16%) | 3 / 592 (0.51%) |
| occurrences causally related to treatment / all | 1 / 3           | 2 / 4            | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| empyema   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| encephalitis viral                              |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| endocarditis                                    |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 2 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| endocarditis bacterial                          |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| enteritis infectious                            |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

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| enterobacter pneumonia<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| enterocolitis infectious<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| erysipelas<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| escherichia sepsis<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| extrapulmonary tuberculosis<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| fascial infection<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| gangrene<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gastroenteritis                                 |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 1 / 297 (0.34%) | 7 / 2579 (0.27%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 1 / 1           | 2 / 7            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gastroenteritis norovirus                       |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gastroenteritis salmonella                      |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| gastroenteritis viral                           |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 1           |
| groin abscess                                   |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| h1n1 influenza                                  |                 |                  |                 |
| alternative dictionary used: MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                     | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |

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|---|-----------------|-------------------|-----------------|
| haematoma infection<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                   |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                  | 0 / 1           | 0 / 1             | 0 / 0           |
| deaths causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0             | 0 / 0           |
| helicobacter gastritis<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                  | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0             | 0 / 0           |
| hepatitis e<br>alternative dictionary used:<br>MedDRA 23.1                          |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                                  | 0 / 0           | 0 / 1             | 0 / 0           |
| deaths causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0             | 0 / 0           |
| herpes zoster infection neurological<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                  | 0 / 0           | 0 / 0             | 1 / 1           |
| deaths causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0             | 0 / 0           |
| herpes zoster<br>alternative dictionary used:<br>MedDRA 23.1                        |                 |                   |                 |
| subjects affected / exposed   | 5 / 297 (1.68%) | 15 / 2579 (0.58%) | 2 / 592 (0.34%) |
| occurrences causally related to<br>treatment / all                                  | 4 / 5           | 20 / 20           | 3 / 3           |
| deaths causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0             | 0 / 0           |
| herpes zoster meningitis<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                   |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%)  | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                                  | 0 / 0           | 0 / 0             | 1 / 1           |
| deaths causally related to<br>treatment / all                                       | 0 / 0           | 0 / 0             | 0 / 0           |
| histoplasmosis<br>alternative dictionary used:<br>MedDRA 23.1                       |                 |                   |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| implant site infection<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| incision site cellulitis<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| infected dermal cyst<br>alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| infected skin ulcer<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 1 / 1           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| infection<br>alternative dictionary used:<br>MedDRA 23.1                   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| infectious pleural effusion<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                            | 0 / 0           | 3 / 3            | 1 / 1           |
| deaths causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |



|  |                 |                  |                 |
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| infective aneurysm<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| influenza<br>alternative dictionary used:<br>MedDRA 23.1                         |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 1 / 1           | 1 / 4            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| intervertebral discitis<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| klebsiella bacteraemia<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| localised infection<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| lower respiratory tract infection<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                               | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to<br>treatment / all                                    | 0 / 0           | 0 / 0            | 0 / 0           |
| lung abscess<br>alternative dictionary used:<br>MedDRA 23.1                      |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| lymph node tuberculosis<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| meningoencephalitis bacterial<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| necrotising fasciitis<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| ophthalmic herpes zoster<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 2 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| oral fungal infection<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 2 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |
| orchitis<br>alternative dictionary used:<br>MedDRA 23.1                      |                 |                  |                 |
| subjects affected / exposed <sup>[36]</sup>                                  | 0 / 66 (0.00%)  | 1 / 548 (0.18%)  | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                              | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                   | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| osteomyelitis<br>alternative dictionary used:<br>MedDRA 23.1              |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 1            | 1 / 1           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| otitis media<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 3 / 3           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| paracoccidioides infection<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| paronychia<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| pelvic abscess<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| perirectal abscess<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                        | 0 / 0           | 0 / 0            | 0 / 2           |
| deaths causally related to<br>treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| peritonitis<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |

|  |                  |                   |                  |
|--|------------------|-------------------|------------------|
| subjects affected / exposed  | 0 / 297 (0.00%)  | 1 / 2579 (0.04%)  | 0 / 592 (0.00%)  |
| occurrences causally related to treatment / all                                | 0 / 0            | 1 / 1             | 0 / 0            |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0             | 0 / 0            |
| plasmodium falciparum infection<br>alternative dictionary used:<br>MedDRA 23.1 |                  |                   |                  |
| subjects affected / exposed  | 0 / 297 (0.00%)  | 1 / 2579 (0.04%)  | 0 / 592 (0.00%)  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0             | 0 / 0            |
| plasmodium vivax infection<br>alternative dictionary used:<br>MedDRA 23.1      |                  |                   |                  |
| subjects affected / exposed  | 0 / 297 (0.00%)  | 1 / 2579 (0.04%)  | 0 / 592 (0.00%)  |
| occurrences causally related to treatment / all                                | 0 / 0            | 0 / 1             | 0 / 0            |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0             | 0 / 0            |
| pneumonia<br>alternative dictionary used:<br>MedDRA 23.1                       |                  |                   |                  |
| subjects affected / exposed  | 15 / 297 (5.05%) | 34 / 2579 (1.32%) | 10 / 592 (1.69%) |
| occurrences causally related to treatment / all                                | 11 / 17          | 20 / 36           | 11 / 14          |
| deaths causally related to treatment / all                                     | 0 / 0            | 1 / 1             | 0 / 1            |
| pneumonia bacterial<br>alternative dictionary used:<br>MedDRA 23.1             |                  |                   |                  |
| subjects affected / exposed  | 0 / 297 (0.00%)  | 1 / 2579 (0.04%)  | 1 / 592 (0.17%)  |
| occurrences causally related to treatment / all                                | 0 / 0            | 1 / 1             | 0 / 1            |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0             | 0 / 0            |
| pneumonia cryptococcal<br>alternative dictionary used:<br>MedDRA 23.1          |                  |                   |                  |
| subjects affected / exposed  | 1 / 297 (0.34%)  | 0 / 2579 (0.00%)  | 0 / 592 (0.00%)  |
| occurrences causally related to treatment / all                                | 1 / 1            | 0 / 0             | 0 / 0            |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0             | 0 / 0            |
| pneumonia influenzal<br>alternative dictionary used:<br>MedDRA 23.1            |                  |                   |                  |
| subjects affected / exposed  | 2 / 297 (0.67%)  | 0 / 2579 (0.00%)  | 1 / 592 (0.17%)  |
| occurrences causally related to treatment / all                                | 3 / 3            | 0 / 0             | 0 / 1            |
| deaths causally related to treatment / all                                     | 0 / 0            | 0 / 0             | 0 / 0            |

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| pneumonia viral<br>alternative dictionary used:<br>MedDRA 23.1               |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| pneumonia legionella<br>alternative dictionary used:<br>MedDRA 23.1          |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| post procedural infection<br>alternative dictionary used:<br>MedDRA 23.1     |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| postoperative abscess<br>alternative dictionary used:<br>MedDRA 23.1         |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| postoperative wound infection<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 1           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| pseudomonal bacteraemia<br>alternative dictionary used:<br>MedDRA 23.1       |                 |                  |                 |
| subjects affected / exposed  | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all                           | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to<br>treatment / all                                | 0 / 0           | 0 / 0            | 0 / 0           |
| psoas abscess<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |                  |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                      | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| pulmonary tuberculosis<br>alternative dictionary used:<br>MedDRA 23.1                |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                      | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| pyelonephritis<br>alternative dictionary used:<br>MedDRA 23.1                        |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 4 / 592 (0.68%) |
| occurrences causally related to treatment / all                                      | 0 / 0           | 1 / 3            | 3 / 4           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| pyelitis<br>alternative dictionary used:<br>MedDRA 23.1                              |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| pyelonephritis acute<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed  | 2 / 297 (0.67%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                      | 0 / 5           | 2 / 2            | 0 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| respiratory syncytial virus infection<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |
| respiratory tract infection<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed  | 2 / 297 (0.67%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                      | 2 / 2           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 0           | 0 / 0            | 0 / 0           |

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| salpingitis  |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed <sup>[37]</sup>        | 0 / 231 (0.00%) | 1 / 2031 (0.05%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 1             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| sepsis   |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 3 / 297 (1.01%) | 10 / 2579 (0.39%) | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 2 / 4           | 5 / 10            | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 2 / 3             | 0 / 0           |  |
| septic shock                                       |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 4 / 2579 (0.16%)  | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 2 / 4             | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 2 / 3             | 0 / 0           |  |
| sinusitis  |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 2 / 2             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| sinusitis bacterial                                |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| skin infection                                     |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| staphylococcal bacteraemia                         |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| staphylococcal sepsis<br>alternative dictionary used:<br>MedDRA 23.1   |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| subcutaneous abscess<br>alternative dictionary used:<br>MedDRA 23.1    |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| systemic infection<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| testicular abscess<br>alternative dictionary used:<br>MedDRA 23.1      |                 |                  |                 |
| subjects affected / exposed <sup>[38]</sup>                            | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 152 (0.66%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 0 / 0            | 1 / 1           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| thrombophlebitis septic<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |
| tooth abscess<br>alternative dictionary used:<br>MedDRA 23.1           |                 |                  |                 |
| subjects affected / exposed  | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                        | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all                             | 0 / 0           | 0 / 0            | 0 / 0           |



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| tuberculosis                                       |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 1 / 1             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| upper respiratory tract infection                  |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 4 / 2579 (0.16%)  | 1 / 592 (0.17%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 2 / 4             | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| urinary tract infection                            |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 4 / 297 (1.35%) | 12 / 2579 (0.47%) | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 3 / 7           | 7 / 12            | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| urinary tract infection bacterial                  |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 2 / 297 (0.67%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 2           | 0 / 0             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| urinary tract infection enterococcal               |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 0 / 2579 (0.00%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0             | 0 / 0           |  |
| urosepsis  |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |
| subjects affected / exposed                        | 1 / 297 (0.34%) | 4 / 2579 (0.16%)  | 0 / 592 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 1 / 1           | 0 / 6             | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 1             | 0 / 0           |  |
| varicella  |                 |                   |                 |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                   |                 |  |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 1 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| varicella zoster virus infection<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| viral infection<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 2            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| vulvitis<br>alternative dictionary used:<br>MedDRA 23.1                         |                 |                  |                 |
| subjects affected / exposed <sup>[39]</sup>                                     | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 440 (0.23%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 2 / 2           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| wound abscess<br>alternative dictionary used:<br>MedDRA 23.1                    |                 |                  |                 |
| subjects affected / exposed   | 1 / 297 (0.34%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| wound sepsis<br>alternative dictionary used:<br>MedDRA 23.1                     |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |
| wound infection<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                                 | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                                      | 0 / 0           | 0 / 0            | 0 / 0           |

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| Metabolism and nutrition disorders                 |                 |                  |                 |
| dehydration  |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 4 / 2579 (0.16%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 4            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| diabetes mellitus                                  |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 2            | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| diabetic ketoacidosis                              |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 2 / 2579 (0.08%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 2            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| diabetic metabolic decompensation                  |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| electrolyte imbalance                              |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hyperglycaemia                                     |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |
| subjects affected / exposed                        | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 1 / 592 (0.17%) |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0            | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| hyperkalaemia                                      |                 |                  |                 |
| alternative dictionary used:<br>MedDRA 23.1        |                 |                  |                 |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| subjects affected / exposed   | 0 / 297 (0.00%) | 0 / 2579 (0.00%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                         | 0 / 0           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| hypokalaemia<br>alternative dictionary used:<br>MedDRA 23.1             |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 3 / 2579 (0.12%) | 1 / 592 (0.17%) |
| occurrences causally related to treatment / all                         | 0 / 0           | 0 / 3            | 0 / 2           |
| deaths causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| hyponatraemia<br>alternative dictionary used:<br>MedDRA 23.1            |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| obesity<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |                  |                 |
| subjects affected / exposed   | 2 / 297 (0.67%) | 0 / 2579 (0.00%) | 2 / 592 (0.34%) |
| occurrences causally related to treatment / all                         | 0 / 2           | 0 / 0            | 0 / 2           |
| deaths causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |
| type 2 diabetes mellitus<br>alternative dictionary used:<br>MedDRA 23.1 |                 |                  |                 |
| subjects affected / exposed   | 0 / 297 (0.00%) | 1 / 2579 (0.04%) | 0 / 592 (0.00%) |
| occurrences causally related to treatment / all                         | 0 / 0           | 0 / 1            | 0 / 0           |
| deaths causally related to treatment / all                              | 0 / 0           | 0 / 0            | 0 / 0           |

|   |                               |  |  |
|---|-------------------------------|--|--|
| <b>Serious adverse events</b>   | 4 mg Baricitinib<br>Step-Down |  |  |
| Total subjects affected by serious adverse events   |                               |  |  |
| subjects affected / exposed   | 178 / 594 (29.97%)            |  |  |
| number of deaths (all causes)   | 14                            |  |  |
| number of deaths resulting from adverse events  | 5                             |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps)<br>adenocarcinoma of colon<br>alternative dictionary used:<br>MedDRA 23.1 |                               |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |  |
| adenocarcinoma pancreas                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| anaplastic meningioma                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| angiolioma                                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| basal cell carcinoma                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| benign neoplasm of skin                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| benign neoplasm of thyroid gland                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| bladder cancer                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| bowen's disease                                    |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| brain neoplasm                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| breast cancer                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| breast cancer metastatic                           |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| cervix carcinoma                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[1]</sup>         | 0 / 448 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| cervix carcinoma stage 0                           |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed <sup>[2]</sup>  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all   | 0 / 0           |  |  |  |
| deaths causally related to treatment / all  | 0 / 0           |  |  |  |
| clear cell renal cell carcinoma<br>alternative dictionary used:<br>MedDRA 23.1                      |                 |  |  |  |
| subjects affected / exposed   | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all   | 0 / 0           |  |  |  |
| deaths causally related to treatment / all  | 0 / 0           |  |  |  |
| colon adenoma<br>alternative dictionary used:<br>MedDRA 23.1  |                 |  |  |  |
| subjects affected / exposed   | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all   | 0 / 0           |  |  |  |
| deaths causally related to treatment / all  | 0 / 0           |  |  |  |
| colon cancer<br>alternative dictionary used:<br>MedDRA 23.1   |                 |  |  |  |
| subjects affected / exposed   | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all   | 0 / 1           |  |  |  |
| deaths causally related to treatment / all  | 0 / 0           |  |  |  |
| colorectal cancer stage iv<br>alternative dictionary used:<br>MedDRA 23.1                           |                 |  |  |  |
| subjects affected / exposed   | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all   | 1 / 1           |  |  |  |
| deaths causally related to treatment / all  | 0 / 0           |  |  |  |
| diffuse large b-cell lymphoma<br>alternative dictionary used:<br>MedDRA 23.1                        |                 |  |  |  |
| subjects affected / exposed   | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all   | 0 / 2           |  |  |  |
| deaths causally related to treatment / all  | 0 / 0           |  |  |  |
| extranodal marginal zone b-cell lymphoma (malt type)<br>alternative dictionary used:<br>MedDRA 23.1 |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| fibrous histiocytoma                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gallbladder cancer                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |  |
| gastric cancer                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastric neoplasm                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| giant cell tumour of tendon sheath              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| intraductal proliferative breast lesion         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|   |                                   |  |  |  |
|---|-----------------------------------|--|--|--|
| invasive ductal breast carcinoma<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| large granular lymphocytosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all     | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| laryngeal cancer<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                 | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| large intestine fibroma<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| lentigo maligna<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                  | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| leukaemia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                        | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| lipoma<br>alternative dictionary used:<br>MedDRA 23.1   |                                   |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all  | 0 / 0           |  |  |  |
| deaths causally related to treatment / all   | 0 / 0           |  |  |  |
| lung adenocarcinoma stage iv<br>alternative dictionary used:<br>MedDRA 23.1            |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all  | 0 / 0           |  |  |  |
| deaths causally related to treatment / all   | 0 / 0           |  |  |  |
| lung adenocarcinoma<br>alternative dictionary used:<br>MedDRA 23.1                     |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all  | 0 / 0           |  |  |  |
| deaths causally related to treatment / all   | 0 / 0           |  |  |  |
| lung cancer metastatic<br>alternative dictionary used:<br>MedDRA 23.1                  |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all  | 0 / 0           |  |  |  |
| deaths causally related to treatment / all   | 0 / 0           |  |  |  |
| lung neoplasm<br>alternative dictionary used:<br>MedDRA 23.1                           |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all  | 0 / 0           |  |  |  |
| deaths causally related to treatment / all   | 0 / 0           |  |  |  |
| lung neoplasm malignant<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all  | 0 / 0           |  |  |  |
| deaths causally related to treatment / all   | 0 / 0           |  |  |  |
| lung squamous cell carcinoma metastatic<br>alternative dictionary used:<br>MedDRA 23.1 |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| lymphocytic leukaemia                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| lymphoproliferative disorder                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| malignant fibrous histiocytoma                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| malignant glioma                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| malignant melanoma                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 3 / 4           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| malignant melanoma in situ                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                                   |  |  |  |
|--|-----------------------------------|--|--|--|
| malignant peritoneal neoplasm<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all           | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| malignant pleural effusion<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all              | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| meningioma<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                              | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| metastases to central nervous<br>system<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| metastases to peritoneum<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| metastatic gastric cancer<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all               | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| mucoepidermoid carcinoma<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| mueller's mixed tumour                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[3]</sup>      | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| neoplasm malignant                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| neuroendocrine carcinoma of the skin            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| non-hodgkin's lymphoma                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| non-small cell lung cancer metastatic           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| nonkeratinising carcinoma of nasopharynx        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| oesophageal squamous cell carcinoma             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| oral neoplasm benign                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ovarian adenoma                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[4]</sup>      | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ovarian cancer                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[5]</sup>      | 1 / 448 (0.22%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ovarian cancer stage iv                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[6]</sup>      | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ovarian germ cell teratoma benign               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed <sup>[7]</sup>      | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| paget's disease of nipple                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pancreatic carcinoma                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pancreatic carcinoma metastatic                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pancreatic carcinoma stage iv                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| papillary cystadenoma lymphomatosum             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| papillary thyroid cancer                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| prostate cancer                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[8]</sup>      | 0 / 146 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| prostate cancer metastatic                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[9]</sup>      | 1 / 146 (0.68%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| prostatic adenoma                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[10]</sup>     | 1 / 146 (0.68%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| rectal cancer                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| renal cancer                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| renal cell carcinoma                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|   |                                   |  |  |  |
|---|-----------------------------------|--|--|--|
| skin cancer<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| small cell lung cancer metastatic<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                        | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| squamous cell carcinoma<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                  | 1 / 594 (0.17%)<br>1 / 1<br>0 / 0 |  |  |  |
| squamous cell carcinoma of lung<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                          | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| squamous cell carcinoma of skin<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                          | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| squamous cell carcinoma of the<br>cervix<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[11]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| squamous cell carcinoma of the<br>parotid gland<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| t-cell lymphoma                                 |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| thyroid cancer stage i                          |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| uterine carcinoma in situ                       |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed <sup>[12]</sup>     | 0 / 448 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| uterine cancer                                  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed <sup>[13]</sup>     | 0 / 448 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| uterine leiomyoma                               |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed <sup>[14]</sup>     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vascular disorders                              |                 |  |  |
| aortic arteriosclerosis                         |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| deep vein thrombosis                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 4 / 594 (0.67%) |  |  |  |
| occurrences causally related to treatment / all | 4 / 4           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| embolism arterial                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| essential hypertension                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| haematoma                                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| haemorrhage                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| hypertensive crisis                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| hypertension                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| hypotension  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| hypovolaemic shock                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| intermittent claudication                          |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| jugular vein thrombosis                            |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| necrosis ischaemic                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| peripheral artery stenosis                         |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| peripheral ischaemia                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| peripheral venous disease                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| rheumatoid vasculitis                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| thrombophlebitis                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| thrombosed varicose vein                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| varicose vein                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|   |  |  |  |  |
|---|--|--|--|--|
| <p>vasculitis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>   | <p>0 / 594 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |  |
| <p>venous thrombosis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>                                  | <p>0 / 594 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |  |
| <p>venous thrombosis limb</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>                             | <p>0 / 594 (0.00%)</p> <p>0 / 0</p> <p>0 / 0</p> |  |  |  |
| <p>Surgical and medical procedures</p> <p>arthrodesis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p> | <p>1 / 594 (0.17%)</p> <p>0 / 1</p> <p>0 / 0</p> |  |  |  |
| <p>cataract operation</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>                                 | <p>1 / 594 (0.17%)</p> <p>0 / 1</p> <p>0 / 0</p> |  |  |  |
| <p>finger amputation</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences causally related to<br/>treatment / all</p> <p>deaths causally related to<br/>treatment / all</p>                                  | <p>1 / 594 (0.17%)</p> <p>0 / 1</p> <p>0 / 0</p> |  |  |  |
| <p>hysterectomy</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p>   |  |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| subjects affected / exposed <sup>[15]</sup>                                  | 0 / 448 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                              | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                   | 0 / 0           |  |  |  |
| internal fixation of fracture<br>alternative dictionary used:<br>MedDRA 23.1 |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                              | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                   | 0 / 0           |  |  |  |
| joint arthroplasty<br>alternative dictionary used:<br>MedDRA 23.1            |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                              | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                   | 0 / 0           |  |  |  |
| knee arthroplasty<br>alternative dictionary used:<br>MedDRA 23.1             |                 |  |  |  |
| subjects affected / exposed  | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all                              | 0 / 1           |  |  |  |
| deaths causally related to treatment / all                                   | 0 / 0           |  |  |  |
| limb reconstructive surgery<br>alternative dictionary used:<br>MedDRA 23.1   |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                              | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                   | 0 / 0           |  |  |  |
| rehabilitation therapy<br>alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                              | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                   | 0 / 0           |  |  |  |
| scar excision<br>alternative dictionary used:<br>MedDRA 23.1                 |                 |  |  |  |
| subjects affected / exposed  | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                              | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                   | 0 / 0           |  |  |  |

|  |                                   |  |  |
|--|-----------------------------------|--|--|
| shoulder arthroplasty<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| vaginal cyst excision<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[16]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Pregnancy, puerperium and perinatal<br>conditions<br>abortion spontaneous<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[17]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| pregnancy<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[18]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 448 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| General disorders and administration<br>site conditions<br>adverse drug reaction<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| alcohol interaction<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| chest pain   |                                   |  |  |



|  |                 |  |  |  |
|--|-----------------|--|--|--|
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| complication associated with device                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| death  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 1           |  |  |  |
| exercise tolerance decreased                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| general physical health deterioration              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| mucosal inflammation                               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 2 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| multiple organ dysfunction syndrome                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| non-cardiac chest pain                          |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| pain  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| pyrexia   |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| sudden cardiac death                            |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| systemic inflammatory response syndrome         |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Immune system disorders                         |                 |  |  |
| anaphylactic reaction                           |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| hypersensitivity                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Social circumstances                            |                 |  |  |
| respite care                                    |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Reproductive system and breast disorders        |                 |  |  |
| adnexa uteri cyst                               |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed <sup>[19]</sup>     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| bartholin's cyst                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed <sup>[20]</sup>     | 1 / 448 (0.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| benign prostatic hyperplasia                    |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed <sup>[21]</sup>     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| cervical cyst                                   |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed <sup>[22]</sup>     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cervical dysplasia                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[23]</sup>     | 1 / 448 (0.22%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| dysfunctional uterine bleeding                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[24]</sup>     | 1 / 448 (0.22%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| endometrial hyperplasia                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[25]</sup>     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| endometrial hypertrophy                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[26]</sup>     | 1 / 448 (0.22%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| endometriosis                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[27]</sup>     | 0 / 448 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| genital prolapse                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| metrorrhagia                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[28]</sup>        | 1 / 448 (0.22%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 3           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| ovarian cyst                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[29]</sup>        | 1 / 448 (0.22%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pelvic pain  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| testicular cyst                                    |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[30]</sup>        | 1 / 146 (0.68%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| uterine polyp                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[31]</sup>        | 1 / 448 (0.22%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| uterine prolapse                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[32]</sup>        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| vaginal haemorrhage                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed <sup>[33]</sup>     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| vaginal prolapse                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed <sup>[34]</sup>     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| acute pulmonary oedema                          |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| acute respiratory distress syndrome             |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| acute respiratory failure                       |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 1 / 2           |  |  |
| allergic bronchitis                             |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| asthma  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| atelectasis                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| bronchitis chronic                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| bronchopneumopathy                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| bronchospasm                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| chronic obstructive pulmonary disease           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cough   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| interstitial lung disease                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 3           |  |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |  |
| lung disorder                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| nasal polyps                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| obstructive airways disorder                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| organising pneumonia                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pleural effusion                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |                 |  |  |  |
|--|-----------------|--|--|--|
| pleurisy   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pneumonia aspiration                               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pneumonitis  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pneumothorax                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pulmonary arterial hypertension                    |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pulmonary embolism                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 3 / 594 (0.51%) |  |  |  |
| occurrences causally related to<br>treatment / all | 3 / 3           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pulmonary hypertension                             |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pulmonary mass                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pulmonary oedema                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| respiratory failure                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| respiratory arrest                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| sleep apnoea syndrome                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| vocal cord polyp                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| Psychiatric disorders                              |                 |  |  |  |
| anxiety  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| confusional state                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| depressed mood                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| depression   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| mental disorder                                    |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| mental status changes                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| suicidal ideation                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| suicide attempt                                 |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Product issues                                  |                 |  |  |
| device dislocation                              |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| device failure                                  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| device loosening                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| bile duct stone                                 |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| biliary colic                                   |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                  |  |  |  |
|---|------------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| biliary obstruction                             |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%)  |  |  |  |
| occurrences causally related to treatment / all | 1 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| cholangitis                                     |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| cholecystitis                                   |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 3 / 594 (0.51%)  |  |  |  |
| occurrences causally related to treatment / all | 1 / 5            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| cholecystitis chronic                           |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| cholecystitis acute                             |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| cholelithiasis                                  |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 10 / 594 (1.68%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 10           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |

|  |                                   |  |  |  |
|--|-----------------------------------|--|--|--|
| gallbladder polyp<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| hepatic cirrhosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| liver disorder<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| nonalcoholic fatty liver disease<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                            | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| Investigations<br>blood creatine phosphokinase<br>increased<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| blood glucose increased<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                     | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| blood pressure increased<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cardiac murmur                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| electrocardiogram t wave inversion              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| electrocardiogram change                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| glomerular filtration rate decreased            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| haemoglobin decreased                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| influenza a virus test positive                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| mycobacterium tuberculosis complex                 |                 |  |  |  |
| test positive                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| transaminases increased                            |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Injury, poisoning and procedural complications     |                 |  |  |  |
| accident   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| ankle fracture                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| brain herniation                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| burns second degree                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| carbon monoxide poisoning                          |                 |  |  |  |
| alternative dictionary used:                       |                 |  |  |  |



|   |                 |  |  |  |
|---|-----------------|--|--|--|
| MedDRA 23.1                                     |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cervical vertebral fracture                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| colon injury                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| compression fracture                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| contusion                                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| crush injury                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| dislocation of vertebra                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| epiphyseal injury                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| face injury                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| fall  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 3 / 594 (0.51%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| femoral neck fracture                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| femur fracture                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| fibula fracture                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| foot fracture                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| hand fracture                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| head injury  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| hip fracture                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| humerus fracture                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 3 / 594 (0.51%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 3           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| injury   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| joint dislocation                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| joint injury                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| keratorhexis                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ligament rupture                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| lower limb fracture                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| lumbar vertebral fracture                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| meniscus injury                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| open globe injury                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| open fracture                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| overdose   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| patella fracture                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pelvic fracture                                    |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| periprosthetic fracture                            |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| post procedural haematoma                          |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| post procedural complication                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| post procedural haemorrhage                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| radius fracture                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| rib fracture                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| road traffic accident                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| scapula fracture                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| seroma   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| skin wound   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| skull fracture                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| spinal compression fracture                        |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| suture rupture                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| synovial rupture                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| tendon injury                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| tendon rupture                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| thoracic vertebral fracture                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| tibia fracture                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 4 / 594 (0.67%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 7           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| toxicity to various agents                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| traumatic arthritis                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| upper limb fracture                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |                                   |  |  |
|--|-----------------------------------|--|--|
| wound<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| wound dehiscence<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| wrist fracture<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Congenital, familial and genetic disorders<br>congenital central nervous system anomaly<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| hydrocele<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[35]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| hypertrophic cardiomyopathy<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Cardiac disorders  |                                   |  |  |

|   |                                   |  |  |  |
|---|-----------------------------------|--|--|--|
| acute coronary syndrome<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| acute left ventricular failure<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| acute myocardial infarction<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | 1 / 594 (0.17%)<br>0 / 1<br>0 / 1 |  |  |  |
| angina pectoris<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| angina unstable<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| aortic valve disease<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all           | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| aortic valve incompetence<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| aortic valve stenosis                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| arteriosclerosis coronary artery                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| atrial fibrillation                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 3 / 594 (0.51%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 4           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| atrial tachycardia                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| atrioventricular block complete                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| bradycardia                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|   |                                   |  |  |  |
|---|-----------------------------------|--|--|--|
| bundle branch block left<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| cardiac arrest<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all             | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| cardiac failure<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all            | 2 / 594 (0.34%)<br>0 / 5<br>0 / 2 |  |  |  |
| cardiac failure acute<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all      | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| cardiac failure chronic<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | 1 / 594 (0.17%)<br>0 / 2<br>0 / 0 |  |  |  |
| cardiac failure congestive<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 594 (0.17%)<br>0 / 1<br>0 / 1 |  |  |  |
| cardio-respiratory arrest<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed   | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                                 | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                      | 0 / 0           |  |  |  |
| chronic left ventricular failure<br>alternative dictionary used:<br>MedDRA 23.1 |                 |  |  |  |
| subjects affected / exposed   | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                                 | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                      | 0 / 0           |  |  |  |
| coronary artery disease<br>alternative dictionary used:<br>MedDRA 23.1          |                 |  |  |  |
| subjects affected / exposed   | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all                                 | 0 / 1           |  |  |  |
| deaths causally related to treatment / all                                      | 0 / 0           |  |  |  |
| coronary artery occlusion<br>alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed   | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                                 | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                      | 0 / 0           |  |  |  |
| coronary artery stenosis<br>alternative dictionary used:<br>MedDRA 23.1         |                 |  |  |  |
| subjects affected / exposed   | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                                 | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                      | 0 / 0           |  |  |  |
| mitral valve disease<br>alternative dictionary used:<br>MedDRA 23.1             |                 |  |  |  |
| subjects affected / exposed   | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all                                 | 0 / 0           |  |  |  |
| deaths causally related to treatment / all                                      | 0 / 0           |  |  |  |
| mitral valve incompetence<br>alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed   | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all                                 | 0 / 2           |  |  |  |
| deaths causally related to treatment / all                                      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| myocardial infarction                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| myocardial ischaemia                               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| palpitations                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pericarditis                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| right ventricular failure                          |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| sinus node dysfunction                             |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| sinus tachycardia                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| stress cardiomyopathy                           |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| supraventricular tachycardia                    |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| ventricular arrhythmia                          |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| ventricular fibrillation                        |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| ventricular tachycardia                         |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nervous system disorders                        |                 |  |  |
| amyotrophic lateral sclerosis                   |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| autonomic neuropathy                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| basal ganglia haemorrhage                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| central nervous system vasculitis               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cerebellar infarction                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cerebellar stroke                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cerebral artery stenosis                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|   |                                   |  |  |  |
|---|-----------------------------------|--|--|--|
| cerebral artery thrombosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| cerebral haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all       | 1 / 594 (0.17%)<br>0 / 1<br>0 / 1 |  |  |  |
| cerebral infarction<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 2 / 594 (0.34%)<br>0 / 2<br>0 / 0 |  |  |  |
| cerebral microhaemorrhage<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| cerebral thrombosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 1 / 594 (0.17%)<br>1 / 1<br>0 / 0 |  |  |  |
| cerebral venous thrombosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| cerebrospinal fistula<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cerebrospinal fluid leakage                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cerebrovascular accident                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cerebrovascular disorder                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cervical cord compression                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cervical radiculopathy                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| dementia  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|   |                                   |  |  |  |
|---|-----------------------------------|--|--|--|
| depressed level of consciousness<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| dizziness<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                        | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| embolic stroke<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| epilepsy<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                         | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| haemorrhage intracranial<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all         | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| haemorrhagic stroke<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all              | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| headache<br>alternative dictionary used:<br>MedDRA 23.1   |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| hemiparesis                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| intercostal neuralgia                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| intracranial aneurysm                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ischaemic cerebral infarction                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ischaemic stroke                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| leukoencephalopathy                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| loss of consciousness                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| metabolic encephalopathy                           |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| migraine   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| myelopathy   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| neuralgia  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| neuropathy peripheral                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| peripheral sensorimotor neuropathy                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| post herpetic neuralgia                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| presyncope                                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| radiculopathy                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| sciatica  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| seizure   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| sensory disturbance                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                                   |  |  |  |
|--|-----------------------------------|--|--|--|
| subarachnoid haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                        | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| syncope<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| thalamus haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                            | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| transient ischaemic attack<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                      | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| Blood and lymphatic system disorders<br>anaemia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 3 / 594 (0.51%)<br>2 / 5<br>0 / 0 |  |  |  |
| coagulopathy<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                    | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| febrile neutropenia<br>alternative dictionary used:<br>MedDRA 23.1   |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| leukocytosis                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| lymphopenia                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| normochromic normocytic anaemia                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| normocytic anaemia                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pancytopenia                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| thrombocytopenia                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |                 |  |  |  |
|--|-----------------|--|--|--|
| thrombocytosis                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Ear and labyrinth disorders                        |                 |  |  |  |
| conductive deafness                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| deafness unilateral                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| meniere's disease                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| sudden hearing loss                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| vertigo  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| vertigo positional                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Eye disorders                                   |                 |  |  |
| cataract  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| cataract subcapsular                            |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| corneal perforation                             |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| dry age-related macular degeneration            |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| glaucoma  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| keratitis                                       |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| macular rupture                                 |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| ocular hypertension                             |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| retinal detachment                              |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| rhegmatogenous retinal detachment               |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| abdominal pain                                  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| abdominal pain upper                            |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| abdominal wall haematoma                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| anal fistula                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| colitis   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| colitis ischaemic                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| colitis ulcerative                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| dental cyst                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| diarrhoea  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| diverticular perforation                           |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| diverticulum                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| diverticulum intestinal                            |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| duodenal ulcer haemorrhage                         |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| duodenitis   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| dysphagia  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| enterocolitis                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastric ulcer                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastric ulcer haemorrhage                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastritis                                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastric ulcer perforation                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastritis erosive                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|   |                                   |  |  |  |
|---|-----------------------------------|--|--|--|
| gastrointestinal haemorrhage<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all     | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| gastrooesophageal reflux disease<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| haemorrhoids<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                     | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| hiatus hernia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                    | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| ileus<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                            | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| inguinal hernia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                  | 1 / 594 (0.17%)<br>0 / 2<br>0 / 0 |  |  |  |
| intestinal obstruction<br>alternative dictionary used:<br>MedDRA 23.1   |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| intestinal perforation                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| irritable bowel syndrome                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| obstructive pancreatitis                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| oesophageal stenosis                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pancreatitis acute                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| parotid gland enlargement                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |                 |  |  |  |
|--|-----------------|--|--|--|
| rectal haemorrhage                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| rectal polyp                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| reflux gastritis                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| small intestinal obstruction                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| upper gastrointestinal haemorrhage                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| umbilical hernia                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| volvulus   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| vomiting  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |
| actinic keratosis                               |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| angioedema                                      |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| diabetic ulcer                                  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| eczema asteatotic                               |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| granuloma skin                                  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| skin ulcer                                      |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| skin necrosis                                   |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| acute kidney injury                             |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| bladder prolapse                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| calculus bladder                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| calculus urinary                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| chronic kidney disease                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| glomerulonephritis membranous                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| hydronephrosis                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| iga nephropathy                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| nephrolithiasis                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| oliguria  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| proteinuria  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| renal colic  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| renal cyst   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| renal injury                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| renal pain   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| renal vein thrombosis                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| stress urinary incontinence                        |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| tubulointerstitial nephritis                    |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| ureterolithiasis                                |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| urinary tract inflammation                      |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Endocrine disorders                             |                 |  |  |
| adrenal suppression                             |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| goitre  |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| hyperparathyroidism                             |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| acquired claw toe                               |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| arthralgia                                      |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| arthritis                                       |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| back pain                                       |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| cervical spinal stenosis                        |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| chondrocalcinosis pyrophosphate                 |                 |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| diastasis recti abdominis                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| foot deformity                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 6 / 594 (1.01%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 7           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| fracture delayed union                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| haematoma muscle                                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| intervertebral disc compression                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| intervertebral disc degeneration                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |   |  |  |  |
|--|---|--|--|--|
| intervertebral disc disorder<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | <br><br>1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| intervertebral disc protrusion<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | <br><br>2 / 594 (0.34%)<br>0 / 2<br>0 / 0 |  |  |  |
| joint destruction<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all               | <br><br>0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| lumbar spinal stenosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | <br><br>1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| mixed connective tissue disease<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | <br><br>0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| muscular weakness<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all               | <br><br>0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| musculoskeletal chest pain<br>alternative dictionary used:<br>MedDRA 23.1  |   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| osteoarthritis                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 5 / 594 (0.84%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 5           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| osteochondrosis                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| osteonecrosis                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| osteoporosis                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| osteoporotic fracture                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pain in extremity                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| rhabdomyolysis                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| rheumatoid arthritis                               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 3 / 594 (0.51%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 3           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| rheumatoid nodule                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| rotator cuff syndrome                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| scoliosis  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| spinal osteoarthritis                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| spinal instability                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| spinal pain                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| spinal stenosis                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| spondylolisthesis                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| spondyloarthropathy                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| synovial cyst                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| synovitis                                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| tendonitis   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| tenosynovitis                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 2 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Infections and infestations                        |                 |  |  |  |
| abdominal infection                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| abdominal wall abscess                             |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| abscess intestinal                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| abscess limb                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 3 / 594 (0.51%) |  |  |  |
| occurrences causally related to<br>treatment / all | 2 / 4           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| anal abscess                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| appendicitis perforated                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| appendicitis                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 4 / 594 (0.67%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 4           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| arthritis bacterial                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| arthritis infective                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| atypical pneumonia                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| bacteraemia                                     |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| bacterial infection                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| bone tuberculosis                                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| breast abscess                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| bronchitis   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 5 / 594 (0.84%) |  |  |  |
| occurrences causally related to<br>treatment / all | 6 / 7           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| bronchitis viral                                   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| bursitis infective                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| bursitis infective staphylococcal                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| covid-19  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| covid-19 pneumonia                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cellulitis                                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 4 / 594 (0.67%) |  |  |  |
| occurrences causally related to treatment / all | 4 / 5           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| cholecystitis infective                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| chronic sinusitis                               |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| chronic tonsillitis                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |                 |  |  |  |
|--|-----------------|--|--|--|
| coronavirus infection                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| cystitis   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| cytomegalovirus hepatitis                          |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| cytomegalovirus infection                          |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| dengue fever                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| device related infection                           |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| device related sepsis                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| disseminated tuberculosis                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| diverticulitis                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| empyema   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| encephalitis viral                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| endocarditis                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| endocarditis bacterial                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                                   |  |  |  |
|--|-----------------------------------|--|--|--|
| enteritis infectious<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all        | 1 / 594 (0.17%)<br>1 / 1<br>0 / 0 |  |  |  |
| enterobacter pneumonia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all      | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| enterocolitis infectious<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all    | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| erysipelas<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                  | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| escherichia sepsis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | 1 / 594 (0.17%)<br>1 / 1<br>0 / 0 |  |  |  |
| extrapulmonary tuberculosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 1 / 594 (0.17%)<br>1 / 1<br>0 / 0 |  |  |  |
| fascial infection<br>alternative dictionary used:<br>MedDRA 23.1   |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gangrene  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastroenteritis                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastroenteritis norovirus                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastroenteritis salmonella                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| gastroenteritis viral                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| groin abscess                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| h1n1 influenza                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| haematoma infection                                |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| helicobacter gastritis                             |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| hepatitis e  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| herpes zoster infection neurological               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| herpes zoster                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 5 / 594 (0.84%) |  |  |  |
| occurrences causally related to<br>treatment / all | 4 / 5           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| herpes zoster meningitis                           |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| histoplasmosis                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| implant site infection                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| incision site cellulitis                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| infected dermal cyst                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| infected skin ulcer                             |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| infection                                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                                   |  |  |  |
|--|-----------------------------------|--|--|--|
| infectious pleural effusion<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| infective aneurysm<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all          | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| influenza<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                   | 1 / 594 (0.17%)<br>1 / 1<br>0 / 0 |  |  |  |
| intervertebral discitis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all     | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| klebsiella bacteraemia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all      | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| localised infection<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all         | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| lower respiratory tract infection<br>alternative dictionary used:<br>MedDRA 23.1   |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| lung abscess                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| lymph node tuberculosis                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| meningoencephalitis bacterial                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| necrotising fasciitis                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| ophthalmic herpes zoster                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| oral fungal infection                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |                 |  |  |  |
|--|-----------------|--|--|--|
| orchitis   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[36]</sup>        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| osteomyelitis                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| otitis media                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| paracoccidioides infection                         |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| paronychia   |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pelvic abscess                                     |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| perirectal abscess                                 |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                  |  |  |  |
|---|------------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| peritonitis                                     |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| plasmodium falciparum infection                 |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| plasmodium vivax infection                      |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| pneumonia                                       |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 12 / 594 (2.02%) |  |  |  |
| occurrences causally related to treatment / all | 8 / 15           |  |  |  |
| deaths causally related to treatment / all      | 0 / 2            |  |  |  |
| pneumonia bacterial                             |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |
| pneumonia cryptococcal                          |                  |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                  |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0            |  |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| pneumonia influenzal                               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 2 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pneumonia viral                                    |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pneumonia legionella                               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| post procedural infection                          |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| postoperative abscess                              |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| postoperative wound infection                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| pseudomonal bacteraemia                            |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| psoas abscess                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pulmonary tuberculosis                          |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pyelonephritis                                  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pyelitis  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| pyelonephritis acute                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| respiratory syncytial virus infection           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                                   |  |  |  |
|--|-----------------------------------|--|--|--|
| respiratory tract infection<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| salpingitis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed <sup>[37]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| sepsis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                      | 2 / 594 (0.34%)<br>0 / 2<br>0 / 0 |  |  |  |
| septic shock<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| sinusitis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                   | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| sinusitis bacterial<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all         | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| skin infection<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| staphylococcal bacteraemia                      |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| staphylococcal sepsis                           |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| subcutaneous abscess                            |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| systemic infection                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| testicular abscess                              |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[38]</sup>     | 0 / 146 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| thrombophlebitis septic                         |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| tooth abscess                                      |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| tuberculosis                                       |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 2 / 594 (0.34%) |  |  |  |
| occurrences causally related to<br>treatment / all | 2 / 2           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| upper respiratory tract infection                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| urinary tract infection                            |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 3 / 594 (0.51%) |  |  |  |
| occurrences causally related to<br>treatment / all | 2 / 4           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| urinary tract infection bacterial                  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| urinary tract infection enterococcal               |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                        | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 0           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| urosepsis  |                 |  |  |  |
| alternative dictionary used:<br>MedDRA 23.1        |                 |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |  |
| varicella                                       |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| varicella zoster virus infection                |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| viral infection                                 |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| vulvitis  |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed <sup>[39]</sup>     | 0 / 448 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| wound abscess                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| wound sepsis                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 4 / 4           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |



|  |                                   |  |  |  |
|--|-----------------------------------|--|--|--|
| wound infection<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                   | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| Metabolism and nutrition disorders<br>dehydration<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| diabetes mellitus<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                                 | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| diabetic ketoacidosis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                             | 1 / 594 (0.17%)<br>0 / 1<br>0 / 0 |  |  |  |
| diabetic metabolic decompensation<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                 | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| electrolyte imbalance<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                             | 0 / 594 (0.00%)<br>0 / 0<br>0 / 0 |  |  |  |
| hyperglycaemia<br>alternative dictionary used:<br>MedDRA 23.1  |                                   |  |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| hyperkalaemia                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| hypokalaemia                                    |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| hyponatraemia                                   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 594 (0.17%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| obesity   |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| type 2 diabetes mellitus                        |                 |  |  |  |
| alternative dictionary used: MedDRA 23.1        |                 |  |  |  |
| subjects affected / exposed                     | 0 / 594 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |

Notes:

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

Justification: Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.

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

Justification: Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.



of participants At Risk adjusted accordingly.

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

Justification: Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.

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

Justification: Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.

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

Justification: Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.

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

Justification: Gender specific events occurring only in male or female participants have had the number of participants At Risk adjusted accordingly.

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

| <b>Non-serious adverse events</b>                     | <b>2 mg Baricitinib</b> | <b>4 mg Baricitinib</b> | <b>2 mg Baricitinib<br/>Step-Down</b> |
|---|-------------------------|-------------------------|---------------------------------------|
| Total subjects affected by non-serious adverse events |                         |                         |                                       |
| subjects affected / exposed                           | 234 / 297 (78.79%)      | 1532 / 2579 (59.40%)    | 270 / 592 (45.61%)                    |
| Investigations  |                         |                         |                                       |
| blood creatine phosphokinase increased                |                         |                         |                                       |
| alternative dictionary used: MedDRA 23.1              |                         |                         |                                       |
| subjects affected / exposed                           | 22 / 297 (7.41%)        | 176 / 2579 (6.82%)      | 20 / 592 (3.38%)                      |
| occurrences (all)                                     | 26                      | 229                     | 26                                    |
| Vascular disorders                                    |                         |                         |                                       |
| hypertension  |                         |                         |                                       |
| alternative dictionary used: MedDRA 23.1              |                         |                         |                                       |
| subjects affected / exposed                           | 33 / 297 (11.11%)       | 196 / 2579 (7.60%)      | 38 / 592 (6.42%)                      |
| occurrences (all)                                     | 36                      | 218                     | 38                                    |
| Nervous system disorders                              |                         |                         |                                       |
| headache  |                         |                         |                                       |
| alternative dictionary used: MedDRA 23.1              |                         |                         |                                       |
| subjects affected / exposed                           | 19 / 297 (6.40%)        | 90 / 2579 (3.49%)       | 0 / 592 (0.00%)                       |
| occurrences (all)                                     | 21                      | 106                     | 0                                     |
| Blood and lymphatic system disorders                  |                         |                         |                                       |
| anaemia   |                         |                         |                                       |
| alternative dictionary used: MedDRA 23.1              |                         |                         |                                       |
| subjects affected / exposed                           | 18 / 297 (6.06%)        | 126 / 2579 (4.89%)      | 0 / 592 (0.00%)                       |
| occurrences (all)                                     | 21                      | 156                     | 0                                     |
| General disorders and administration site conditions  |                         |                         |                                       |

|  |  |  |  |
|--|--|--|--|
| pyrexia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)   | 16 / 297 (5.39%)<br>17                                 | 56 / 2579 (2.17%)<br>62                                    | 0 / 592 (0.00%)<br>0                               |
| Gastrointestinal disorders<br>constipation<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)<br><br>diarrhoea<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)  | 20 / 297 (6.73%)<br>24<br><br>18 / 297 (6.06%)<br>25   | 72 / 2579 (2.79%)<br>79<br><br>87 / 2579 (3.37%)<br>107    | 0 / 592 (0.00%)<br>0<br><br>0 / 592 (0.00%)<br>0   |
| Respiratory, thoracic and mediastinal disorders<br>cough<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)  | 28 / 297 (9.43%)<br>46                                 | 105 / 2579 (4.07%)<br>134                                  | 35 / 592 (5.91%)<br>37                             |
| Psychiatric disorders<br>insomnia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)   | 16 / 297 (5.39%)<br>16                                 | 47 / 2579 (1.82%)<br>50                                    | 0 / 592 (0.00%)<br>0                               |
| Musculoskeletal and connective tissue disorders<br>arthralgia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)<br><br>back pain<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)<br><br>pain in extremity<br>alternative dictionary used:<br>MedDRA 23.1 | 43 / 297 (14.48%)<br>58<br><br>42 / 297 (14.14%)<br>55 | 155 / 2579 (6.01%)<br>229<br><br>162 / 2579 (6.28%)<br>181 | 0 / 592 (0.00%)<br>0<br><br>35 / 592 (5.91%)<br>41 |

|  |                         |                               |                         |
|--|-------------------------|-------------------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)   | 16 / 297 (5.39%)<br>25  | 53 / 2579 (2.06%)<br>63       | 0 / 592 (0.00%)<br>0    |
| rheumatoid arthritis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                      | 27 / 297 (9.09%)<br>38  | 141 / 2579 (5.47%)<br>250     | 0 / 592 (0.00%)<br>0    |
| Infections and infestations<br>bronchitis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all) | 48 / 297 (16.16%)<br>65 | 291 / 2579<br>(11.28%)<br>431 | 44 / 592 (7.43%)<br>61  |
| herpes zoster<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                             | 30 / 297 (10.10%)<br>32 | 160 / 2579 (6.20%)<br>167     | 39 / 592 (6.59%)<br>42  |
| influenza<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                                 | 15 / 297 (5.05%)<br>16  | 147 / 2579 (5.70%)<br>176     | 30 / 592 (5.07%)<br>35  |
| nasopharyngitis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                           | 42 / 297 (14.14%)<br>95 | 291 / 2579<br>(11.28%)<br>488 | 54 / 592 (9.12%)<br>109 |
| pharyngitis<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                               | 19 / 297 (6.40%)<br>30  | 119 / 2579 (4.61%)<br>181     | 0 / 592 (0.00%)<br>0    |
| pneumonia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                                 | 17 / 297 (5.72%)<br>19  | 66 / 2579 (2.56%)<br>71       | 0 / 592 (0.00%)<br>0    |
| sinusitis<br>alternative dictionary used:<br>MedDRA 23.1   |                         |                               |                         |

|  |                          |                               |                        |
|--|--------------------------|-------------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 23 / 297 (7.74%)<br>31   | 100 / 2579 (3.88%)<br>121     | 0 / 592 (0.00%)<br>0   |
| upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                           | 58 / 297 (19.53%)<br>106 | 281 / 2579<br>(10.90%)<br>454 | 46 / 592 (7.77%)<br>54 |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                                     | 53 / 297 (17.85%)<br>84  | 241 / 2579 (9.34%)<br>336     | 34 / 592 (5.74%)<br>48 |
| Metabolism and nutrition disorders<br>hypercholesterolaemia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all) | 16 / 297 (5.39%)<br>19   | 142 / 2579 (5.51%)<br>162     | 18 / 592 (3.04%)<br>18 |
| hyperlipidaemia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)   | 18 / 297 (6.06%)<br>20   | 133 / 2579 (5.16%)<br>157     | 0 / 592 (0.00%)<br>0   |

|  |                               |  |  |
|--|-------------------------------|--|--|
| <b>Non-serious adverse events</b>  | 4 mg Baricitinib<br>Step-Down |  |  |
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed  | 315 / 594 (53.03%)            |  |  |
| Investigations<br>blood creatine phosphokinase<br>increased<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all) | 33 / 594 (5.56%)<br>44        |  |  |
| Vascular disorders<br>hypertension<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)                          | 46 / 594 (7.74%)<br>47        |  |  |
| Nervous system disorders   |                               |  |  |



|   |  |  |  |
|---|--|--|--|
| headache<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 594 (0.00%)<br>0                             |  |  |
| Blood and lymphatic system disorders<br>anaemia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 594 (0.00%)<br>0                             |  |  |
| General disorders and administration site conditions<br>pyrexia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 594 (0.00%)<br>0                             |  |  |
| Gastrointestinal disorders<br>constipation<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)<br><br>diarrhoea<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 594 (0.00%)<br>0<br><br>0 / 594 (0.00%)<br>0 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>cough<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)   | 25 / 594 (4.21%)<br>32                           |  |  |
| Psychiatric disorders<br>insomnia<br>alternative dictionary used:<br>MedDRA 23.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 594 (0.00%)<br>0                             |  |  |
| Musculoskeletal and connective tissue disorders   |  |  |  |

|  |   |  |  |
|--|---|--|--|
| <p>arthralgia</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 594 (0.00%)</p> <p>0</p>   |  |  |
| <p>back pain</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>36 / 594 (6.06%)</p> <p>43</p>   |  |  |
| <p>pain in extremity</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 594 (0.00%)</p> <p>0</p>   |  |  |
| <p>rheumatoid arthritis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 594 (0.00%)</p> <p>0</p>   |  |  |
| <p>Infections and infestations</p> <p>bronchitis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>herpes zoster</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>influenza</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>nasopharyngitis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pharyngitis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> | <p>65 / 594 (10.94%)</p> <p>91</p> <p>53 / 594 (8.92%)</p> <p>57</p> <p>56 / 594 (9.43%)</p> <p>64</p> <p>58 / 594 (9.76%)</p> <p>101</p> |  |  |

|  |  |  |  |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 594 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>  |  |  |  |
| <p>pneumonia</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>0 / 594 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>sinusitis</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>0 / 594 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>upper respiratory tract infection</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>51 / 594 (8.59%)</p> <p>occurrences (all)</p> <p>63</p>                               |  |  |  |
| <p>urinary tract infection</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>52 / 594 (8.75%)</p> <p>occurrences (all)</p> <p>72</p>   |  |  |  |
| <p>Metabolism and nutrition disorders</p> <p>hypercholesterolaemia</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>32 / 594 (5.39%)</p> <p>occurrences (all)</p> <p>32</p> |  |  |  |
| <p>hyperlipidaemia</p> <p>alternative dictionary used:<br/>MedDRA 23.1</p> <p>subjects affected / exposed</p> <p>0 / 594 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 21 March 2014    | Amendment (d): Allowed additional enrollment of participants and extend duration of study. |
| 30 October 2014  | Amendment (e): Allowed for additional 24 months of treatment duration.                     |
| 30 January 2017  | Amendment (f): Allowed for additional 12 months of treatment duration.                     |
| 11 December 2017 | Amendment (g): Allowed for an additional 24 months of treatment duration.                  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported