



Clinical trial results:

A Randomized, Observer-blind, Active Comparator-controlled, Multicenter, Phase 3 Study to Assess the Efficacy, Safety, and Immunogenicity of a Plant-derived Quadrivalent VLP Influenza Vaccine in Adults 65 Years of Age and Older

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-001894-26 |
| Trial protocol | DE FI |
| Global end of trial date | 16 July 2019 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 29 September 2023 |
| First version publication date | 29 September 2023 |

Trial information

Trial identification

| | |
|-----------------------|-----------------|
| Sponsor protocol code | CP-PRO-QVLP-014 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03739112 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Medicago |
| Sponsor organisation address | 1020 route de l'Église, bureau 600, Québec, Canada, |
| Public contact | Medical Director, Medicago, +1 418658-9393, clinicaltrialinquiries@medicago.com |
| Scientific contact | Medical Director, Medicago, +1 418658-9393, clinicaltrialinquiries@medicago.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 16 July 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 July 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy, relative to an active comparator, of a single 30 microgram (µg)/strain dose of the Quadrivalent Virus-like Particle (VLP) Influenza Vaccine, against protocol-defined influenza-like illness (ILI) caused by any influenza viral type/subtype (reverse transcription polymerase chain reaction [RT-PCR]).

Protection of trial subjects:

This study was conducted in accordance with the current International Council for Harmonisation (ICH) guidance, Good Clinical Practice (GCP) as established by the ICH (ICH E6 GCP), the European Union Clinical Trials Directive 2001 / 20 / EC, United States (US) 21 Code of Federal Regulations dealing with clinical studies, applicable federal, state, and/or local laws and regulations in the countries where the clinical study was conducted, clinical study contractual obligations, and the principles enunciated in the World Medical Association Declaration of Helsinki.

The Investigator or designee fully informed the subject of the risks and requirements of the study and, during the study, subjects were given any new information that could have affected their decision to continue participation. Subjects were told that their consent to participate in the study was voluntary and that it could be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only subjects who were fully able to understand the risks, benefits, and potential adverse events (AEs) of the study, and who provided their consent voluntarily were enrolled. The Investigator or designee answered all questions prior to requesting the subject's signature on the informed consent form (ICF). Subjects had sufficient time to consider the risks and benefits associated with participation in the study prior to signing the ICF. Each subject signed the ICF containing appropriate study and study drug information and was provided a copy of the ICF.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 18 September 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | Finland: 1329 |
| Country: Number of subjects enrolled | Germany: 2683 |
| Country: Number of subjects enrolled | Thailand: 537 |
| Country: Number of subjects enrolled | Canada: 2517 |
| Country: Number of subjects enrolled | United States: 5728 |
| Worldwide total number of subjects | 12794 |
| EEA total number of subjects | 4012 |

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) | 0 |
| From 65 to 84 years | 12419 |
| 85 years and over | 375 |

Subject disposition

Recruitment

Recruitment details:

Participants were randomized in a 1:1 ratio to receive the Quadrivalent virus-like particle (VLP) Influenza Vaccine at a dose of 30 µg/strain or the active comparator.

Pre-assignment

Screening details:

Participants aged 65 years or older with no acute or evolving medical problems were assessed.

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|----------------------------------|
| Arm title | Quadrivalent (30 µg) VLP Vaccine |
|------------------|----------------------------------|

Arm description:

Participants received one intramuscular (IM) injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0.

| | |
|--|------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Quadrivalent VLP Influenza Vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose of a 30 µg/strain of Quadrivalent VLP Vaccine.

| | |
|------------------|-----------------------------|
| Arm title | Active Comparator (Fluarix) |
|------------------|-----------------------------|

Arm description:

Participants received one IM injection of 0.5 milliliter (mL) of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Fluarix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose of a 15 µg/strain of Fluarix Quadrivalent® Comparator Vaccine.

| Number of subjects in period 1 | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) |
|---------------------------------------|---|------------------------------------|
| Started | 6396 | 6398 |
| Completed | 6196 | 6222 |
| Not completed | 200 | 176 |
| Adverse event, serious fatal | 12 | 16 |
| Consent withdrawn by subject | 38 | 19 |
| Physician decision | 1 | - |
| Site went on hold | 65 | 67 |
| Adverse event, non-fatal | 2 | 2 |
| Randomized but not vaccinated | 31 | 25 |
| Other than specified | 8 | 5 |
| Lost to follow-up | 31 | 33 |
| Protocol deviation | 12 | 9 |

Baseline characteristics

Reporting groups

| | |
|---|----------------------------------|
| Reporting group title | Quadrivalent (30 µg) VLP Vaccine |
| Reporting group description: | |
| Participants received one intramuscular (IM) injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0. | |
| Reporting group title | Active Comparator (Fluarix) |
| Reporting group description: | |
| Participants received one IM injection of 0.5 milliliter (mL) of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0. | |

| Reporting group values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | Total |
|------------------------|----------------------------------|-----------------------------|-------|
| Number of subjects | 6396 | 6398 | 12794 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--|--------|-------|-------|
| Age continuous | | | |
| Baseline characteristics are summarized for the SAS. | | | |
| Units: years | | | |
| arithmetic mean | 72.2 | 72.2 | |
| standard deviation | ± 5.67 | ± 5.7 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 3577 | 3575 | 7152 |
| Male | 2819 | 2823 | 5642 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 202 | 198 | 400 |
| Not Hispanic or Latino | 6179 | 6190 | 12369 |
| Unknown or Not Reported | 15 | 10 | 25 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 19 | 13 | 32 |
| Asian | 308 | 300 | 608 |
| Native Hawaiian or Other Pacific Islander | 5 | 5 | 10 |
| Black or African American | 251 | 266 | 517 |
| White | 5805 | 5803 | 11608 |
| More than one race | 6 | 10 | 16 |
| Unknown or Not Reported | 2 | 1 | 3 |

End points

End points reporting groups

| | |
|---|----------------------------------|
| Reporting group title | Quadrivalent (30 µg) VLP Vaccine |
| Reporting group description: Participants received one intramuscular (IM) injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0. | |
| Reporting group title | Active Comparator (Fluarix) |
| Reporting group description: Participants received one IM injection of 0.5 milliliter (mL) of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0. | |

Primary: Number of occurrences of protocol-defined Influenza-like Illness (ILI) due to any laboratory-confirmed Influenza strains

| | |
|--|--|
| End point title | Number of occurrences of protocol-defined Influenza-like Illness (ILI) due to any laboratory-confirmed Influenza strains |
| End point description: Occurrences of laboratory-confirmed ILI caused by any influenza viral strains was measured by reverse transcriptase polymerase chain reaction (RT-PCR). A participant was considered to have protocol-defined ILI if the participant met at least one of the following pre-defined respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing and at least one of the following systemic symptoms: fever (defined as a temperature > 37.2 °C or > 99.0 °F), chills, tiredness, headache, or myalgia. The number of laboratory-confirmed ILI cases caused by any influenza strains are reported. The Per protocol (PP) set consisted of the participants who participated in the study until at least the end of the peak period or for at least five months or until the end of the surveillance period. | |
| End point type | Primary |
| End point timeframe: Day 14 (post vaccination) up to 9 months | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5996 | 6026 | | |
| Units: Number of cases | | | | |
| number (not applicable) | 118 | 130 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: Vaccine efficacy (VE) of VLP vaccine versus Fluarix = $(1 - \text{ARVv} / \text{ARVc}) \times 100\%$ where ARVv = attack rate in participants vaccinated with the Quadrivalent VLP Influenza vaccine and ARVc = attack rate in participants vaccinated with an active Fluarix. | |
| Comparison groups | Quadrivalent (30 µg) VLP Vaccine v Active Comparator (Fluarix) |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 12022 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| Parameter estimate | percent VE |
| Point estimate | 8.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.7 |
| upper limit | 28.7 |

Notes:

[1] - Non-inferiority was concluded if the lower limit of the two-sided 95% confidence interval (CI) for relative VE was > -20%.

Secondary: Number of occurrences of laboratory confirmed protocol-defined Influenza-like Illness (ILI) caused by vaccine-matched Influenza strains

| | |
|-----------------|---|
| End point title | Number of occurrences of laboratory confirmed protocol-defined Influenza-like Illness (ILI) caused by vaccine-matched Influenza strains |
|-----------------|---|

End point description:

Occurrences of protocol-defined ILI due to laboratory-confirmed influenza caused by influenza viral types/subtypes that were matched (and/or antigenically similar) to the strains covered in the vaccine formulation was measured by sequential RT-PCR & serotyping. The vaccine-matched strains included: homologous A/Michigan/45/2015 [H1N1], homologous A/Singapore/INFIMH-16-0019/2016 [H3N2], homologous B/Colorado/06/2017 and homologous B/Phuket/3073/2013) covered in the vaccine formulation. A participant was considered to have protocol-defined ILI if the participant met at least one of the following pre-defined respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing and at least one of the following systemic symptoms: fever (defined as a temperature > 37.2 °C or > 99.0 °F), chills, tiredness, headache, or myalgia. The number of laboratory-confirmed ILI cases caused by vaccine-matched influenza strains (all matched strains) are reported. PP set.

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

End point timeframe:

Day 14 (post vaccination) up to 9 months

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5996 | 6026 | | |
| Units: Number of cases | | | | |
| number (not applicable) | 42 | 46 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of occurrences of protocol-defined respiratory illness due to any laboratory confirmed Influenza strains

| | |
|-----------------|---|
| End point title | Number of occurrences of protocol-defined respiratory illness due to any laboratory confirmed Influenza strains |
|-----------------|---|

End point description:

Occurrences of protocol-defined respiratory illness due to laboratory-confirmed influenza strain (matched, mismatched, and un-typed) was measured by sequential RT-PCR. A protocol-defined respiratory illness was determined by the occurrence of at least 1 of the following respiratory symptoms: sneezing, stuffy nose, sore throat, cough, sputum production, wheezing, or difficulty breathing. The number of protocol-defined respiratory illness cases caused by any laboratory-confirmed influenza strain (matched, mismatched, and un-typed) are reported. PP set.

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

End point timeframe:

Day 14 (post vaccination) up to 9 months

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5996 | 6026 | | |
| Units: Number of cases | | | | |
| number (not applicable) | 148 | 167 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of occurrences of protocol-defined respiratory illness vaccine caused by vaccine-matched Influenza strains

| | |
|-----------------|---|
| End point title | Number of occurrences of protocol-defined respiratory illness vaccine caused by vaccine-matched Influenza strains |
|-----------------|---|

End point description:

Occurrences of protocol-defined respiratory illness vaccine caused by vaccine-matched influenza strains was measured by sequential RT-PCR & serotyping. The vaccine-matched strains included: homologous A/Michigan/45/2015 [H1N1], homologous A/Singapore/INFIMH-16-0019/2016 [H3N2], homologous B/Colorado/06/2017 and homologous B/Phuket/3073/2013. The protocol-defined respiratory illness was determined by the occurrence of at least 1 of the following respiratory symptoms: sneezing, stuffy nose, sore throat, cough, sputum production, wheezing, or difficulty breathing. The number of protocol-defined respiratory illness cases caused by one or more vaccine-matched strains are reported. PP set.

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

End point timeframe:

Day 14 (post vaccination) up to 9 months

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5996 | 6026 | | |
| Units: Number of cases | | | | |
| number (not applicable) | 50 | 55 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of occurrences of protocol-defined ILI

| | |
|-----------------|---|
| End point title | Number of occurrences of protocol-defined ILI |
|-----------------|---|

End point description:

Occurrences of protocol-defined ILI that were confirmed or not by laboratory testing were assessed. A participant was considered to have protocol-defined ILI if the participant met at least one of the following pre-defined respiratory symptoms: sore throat, cough, sputum production, wheezing, or difficulty breathing and at least one of the following systemic symptoms: fever (defined as a temperature > 37.2 °C or > 99.0 °F), chills, tiredness, headache or myalgia. The number of protocol-defined ILI cases (confirmed or not) are reported. PP set.

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

End point timeframe:

Day 14 (post vaccination) up to 9 months

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5996 | 6026 | | |
| Units: Number of cases | | | | |
| number (not applicable) | 1249 | 1243 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one immediate complaints

| | |
|-----------------|---|
| End point title | Number of participants with at least one immediate complaints |
|-----------------|---|

End point description:

Immediate complaints were defined as any solicited local or systemic reactions. Solicited local reactions included: erythema, swelling, and pain at the injection site) and solicited systemic reactions included: fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in the axilla, and swelling in the neck. Safety Analysis Set (SAS) was defined as all participants who received either the Quadrivalent VLP Influenza Vaccine or the active comparator. Participants that were non-compliant to protocol/Good Clinical Practice (GCP), as per investigator, were excluded from analysis.

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

End point timeframe:

15 minutes post vaccination

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 | 6366 | | |
| Units: Participants | | | | |
| number (not applicable) | 272 | 184 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with ≥ Severe solicited local and systemic reactions

| | |
|--|---|
| End point title | Number of participants with ≥ Severe solicited local and systemic reactions |
| End point description: | |
| Participants were monitored for both solicited local reactions (erythema, swelling, and pain at the injection site) and solicited systemic reactions (fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in the axilla, and swelling in the neck). The intensity of the solicited reactions was graded as mild (1)-easily tolerated and does not interfere with usual activity; moderate (2)-interferes with daily activity, but the participant is still able to function; severe (3)-incapacitating and the participant is unable to work or complete usual activity or potentially life threatening; (4)-likely to be life-threatening if not treated in a timely manner, according to the Food and Drug Administration (FDA) Guidance for Industry. ≥ Severe events included severe and potentially life-threatening events. Any ≥severe solicited reactions are reported. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 0 (post-vaccination) to Day 7 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 ^[2] | 6366 ^[3] | | |
| Units: Participants | | | | |
| number (not applicable) | 47 | 62 | | |

Notes:

[2] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[3] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with ≥ Severe related solicited reactions

| | |
|-----------------|--|
| End point title | Number of participants with ≥ Severe related solicited |
|-----------------|--|

End point description:

Participants were monitored for both solicited local reactions (erythema, swelling, & pain at the injection site) & solicited systemic reactions (fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in axilla, & swelling in neck). The intensity of solicited reactions was graded as mild (1)-easily tolerated and does not interfere with usual activity; moderate (2)-interferes with daily activity, but the participant is still able to function; severe (3)-incapacitating and the participant is unable to work or complete usual activity or potentially life threatening; (4)-likely to be life-threatening if not treated in a timely manner, according to the FDA Guidance for Industry. ≥ Severe events included severe and potentially life-threatening events. Any ≥severe related (possibly related, probably related, and definitely related to the study treatments [as defined by investigator]) solicited events are reported.

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

End point timeframe:

Day 0 (post-vaccination) to Day 7

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 ^[4] | 6366 ^[5] | | |
| Units: Participants | | | | |
| number (not applicable) | 28 | 51 | | |

Notes:

[4] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[5] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with unsolicited Treatment-Emergent Adverse Events (TEAEs)

| | |
|-----------------|---|
| End point title | Number of participants with unsolicited Treatment-Emergent Adverse Events (TEAEs) |
|-----------------|---|

End point description:

Participants were monitored for unsolicited TEAEs (e.g., nasopharyngitis, upper respiratory tract infection, headache, and pain). An adverse event (AE) or adverse experience was defined as any untoward medical occurrence in a participant or clinical investigation participant who received study drug, with or without a causal relationship with the treatment. An AE was considered treatment-emergent if it began on or after the date and time of Study Day 0 vaccination. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

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

End point timeframe:

Day 0 (post-vaccination) to Day 21

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 | 6366 | | |
| Units: Participants | | | | |
| number (not applicable) | 849 | 824 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with ≥ Severe unsolicited TEAEs

| | |
|-----------------|--|
| End point title | Number of participants with ≥ Severe unsolicited TEAEs |
|-----------------|--|

End point description:

Participants were monitored for unsolicited TEAEs (e.g., nasopharyngitis, upper respiratory tract infection, headache, and pain). AE: any untoward medical occurrence in a participant or clinical investigation participant who received study drug, with or without a causal relationship with the treatment. An AE was considered treatment-emergent if it began on or after the date and time of Study Day 0 vaccination. The intensity of the solicited reactions was graded as mild (1)-easily tolerated and does not interfere with usual activity; moderate (2)-interferes with daily activity, but the participant is still able to function; severe (3)-incapacitating and the participant is unable to work or complete usual activity or potentially life threatening; (4)-likely to be life-threatening if not treated in a timely manner, according to the FDA Guidance for Industry. ≥ severe events included severe and potentially life-threatening events. Any ≥ severe unsolicited reactions are reported.

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

End point timeframe:

Day 0 (post-vaccination) to Day 21

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 ^[6] | 6366 ^[7] | | |
| Units: Participants | | | | |
| number (not applicable) | 33 | 34 | | |

Notes:

[6] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[7] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with ≥ Severe related unsolicited reactions

| | |
|-----------------|--|
| End point title | Number of participants with ≥ Severe related unsolicited reactions |
|-----------------|--|

End point description:

Participants were monitored for unsolicited TEAEs (e.g., nasopharyngitis, upper respiratory tract infection, headache, & pain). AE: any untoward medical occurrence in a participant who received study drug, with or without a causal relationship with treatment. An AE was considered treatment-emergent if

it began on or after date & time of Study Day 0 vaccination. Intensity of solicited reactions was graded as mild (1) easily tolerated & not interfere with usual activity; moderate (2) interferes with daily activity, but participant still able to function; severe (3) incapacitating & participant unable to work/complete usual activity/ potentially life threatening; (4) likely to be life-threatening if not treated in a timely manner, according to FDA Guidance for Industry. ≥ severe events included severe & potentially life-threatening events. Any ≥severe related (possibly, probably, & definitely related to study treatments [as defined by investigator]) unsolicited events are reported.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 0 (post-vaccination) to Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 ^[8] | 6366 ^[9] | | |
| Units: Participants | | | | |
| number (not applicable) | 1 | 3 | | |

Notes:

[8] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

[9] - SAS. Participants non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one Serious Adverse Event (SAE)

| | |
|-----------------|--|
| End point title | Number of participants with at least one Serious Adverse Event (SAE) |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a participant who received study drug, with or without a causal relationship with treatment. An SAE was an AE that resulted in death, was life threatening, resulted in a persistent or significant disability or incapacity, resulted in or prolonged an existing hospitalization, was a congenital anomaly or birth defect, or was another important medical event. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 0 to 9 months | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 | 6366 | | |
| Units: Participants | | | | |
| number (not applicable) | 263 | 266 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of occurrences of death

| | |
|-----------------|--------------------------------|
| End point title | Number of occurrences of death |
|-----------------|--------------------------------|

End point description:

The number of participants who died during the study was assessed. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

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

End point timeframe:

Day 0 up to 9 months

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 | 6366 | | |
| Units: Participants | | | | |
| number (not applicable) | 12 | 17 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who withdrew due to an AE

| | |
|-----------------|--|
| End point title | Number of participants who withdrew due to an AE |
|-----------------|--|

End point description:

An AE or adverse experience was defined as any untoward medical occurrence in a participant or clinical investigation participant who received study drug, with or without a causal relationship with the treatment. An AE can be any favorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not related to a medicinal product. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

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

End point timeframe:

Day 0 up to 9 months

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 | 6366 | | |
| Units: Participants | | | | |
| number (not applicable) | 15 | 20 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one New Onset Chronic Diseases (NOCDs)

| | |
|-----------------|---|
| End point title | Number of participants with at least one New Onset Chronic Diseases (NOCDs) |
|-----------------|---|

End point description:

All NOCDs that may plausibly have an allergic, autoimmune or inflammatory component were reported. Plausibility should be interpreted broadly; however, the only clear exceptions were degenerative conditions such as osteoarthritis, age-related physiologic changes and life-style diseases. In this context, most cancers, cardiac conditions and kidney diseases should be reported. NOCDs were collected from vaccination on Day 0 to the end of the surveillance period. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

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

End point timeframe:

Day 0 up to 9 months

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 | 6366 | | |
| Units: Participants | | | | |
| number (not applicable) | 36 | 23 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean titers (GMTs) of Hemagglutination Inhibition (HI) antibody response for each homologous and heterologous Influenza strains

| | |
|-----------------|---|
| End point title | Geometric mean titers (GMTs) of Hemagglutination Inhibition (HI) antibody response for each homologous and heterologous Influenza strains |
|-----------------|---|

End point description:

GMTs were measured using a HI assay for the homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. The Immunogenicity Per Protocol (IPP) set consisted of a subset of participants who participated in the immunogenicity portion of the study and who had a Day 21 immunogenicity sample collection.

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

End point timeframe:
Baseline (Day 0), Day 21

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|---|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Homologous Strain (H1N1): Day 0 | 43.8 (36.3 to 52.7) | 36.3 (30.0 to 43.9) | | |
| Homologous Strain (H1N1): Day 21 | 88.9 (73.7 to 107.2) | 146.8 (121.4 to 177.7) | | |
| Homologous Strain (H3N2): Day 0 | 31.1 (25.5 to 37.8) | 30.9 (25.3 to 37.8) | | |
| Homologous Strain (H3N2): Day 21 | 79.5 (65.2 to 97.1) | 90.2 (73.7 to 110.5) | | |
| Homologous Strain (B/Colorado): Day 0 | 15.5 (13.3 to 18.1) | 13.2 (11.3 to 15.5) | | |
| Homologous Strain (B/Colorado): Day 21 | 23.0 (19.3 to 27.4) | 51.7 (43.3 to 61.8) | | |
| Homologous Strain (B/Phuket): Day 0 | 24.4 (20.8 to 28.7) | 22.6 (19.2 to 26.6) | | |
| Homologous Strain (B/Phuket): Day 21 | 45.0 (37.8 to 53.5) | 75.5 (63.3 to 90.1) | | |
| Heterologous Strain (H1N1): Day 0 | 15.5 (13.6 to 17.6) | 13.5 (11.8 to 15.4) | | |
| Heterologous Strain (H1N1): Day 21 | 16.6 (14.3 to 19.2) | 32.4 (28.0 to 37.6) | | |
| Heterologous Strain (H3N2): Day 0 | 19.5 (16.4 to 23.3) | 22.6 (18.9 to 27.1) | | |
| Heterologous Strain (H3N2): Day 21 | 32.4 (27.1 to 38.6) | 46.6 (38.9 to 55.8) | | |
| Heterologous Strain (B/Malaysia): Day 0 | 12.6 (11.0 to 14.5) | 11.4 (10.0 to 13.1) | | |
| Heterologous Strain (B/Malaysia): Day 21 | 15.9 (13.6 to 18.7) | 34.8 (29.5 to 41.0) | | |
| Heterologous Strain (B/Florida): Day 0 | 22.5 (19.2 to 26.4) | 20.6 (17.5 to 24.2) | | |
| Heterologous Strain (B/Florida): Day 21 | 38.0 (32.2 to 44.8) | 72.1 (61.0 to 85.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with seroconversion measured by HI antibody response for each homologous and heterologous strain

| | |
|-----------------|---|
| End point title | Percentage of participants with seroconversion measured by HI antibody response for each homologous and heterologous strain |
|-----------------|---|

End point description:

The percentage of participants in a given treatment group with either a ≥ 4 -fold increase in reciprocal HI titers between Day 0 and Day 21 or a rise of undetectable HI titer (i.e. < 10) pre-vaccination (Day 0) to an HI titer of ≥ 40 on Day 21 was measured using an HI assay for the homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. IPP set.

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

End point timeframe:

Day 0 (pre-vaccination) to Day 21

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------------|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Homologous Strain (H1N1) | 15.5 (10.9 to 21.2) | 40.7 (33.8 to 47.9) | | |
| Homologous Strain (H3N2) | 25.2 (19.5 to 31.7) | 28.1 (22.0 to 34.9) | | |
| Homologous Strain (B/Colorado) | 10.2 (6.4 to 15.2) | 38.2 (31.4 to 45.3) | | |
| Homologous Strain (B/Phuket) | 16.5 (11.7 to 22.3) | 34.7 (28.1 to 41.7) | | |
| Heterologous Strain (H1N1) | 0.5 (0.0 to 2.7) | 24.1 (18.4 to 30.7) | | |
| Heterologous Strain (H3N2) | 10.7 (6.8 to 15.7) | 14.6 (10.0 to 20.3) | | |
| Heterologous Strain (B/Malaysia) | 5.3 (2.7 to 9.4) | 30.7 (24.3 to 37.6) | | |
| Heterologous Strain (B/Florida) | 12.1 (8.0 to 17.4) | 37.7 (30.9 to 44.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with seroprotection measured by HI antibody response for each homologous and heterologous strain

| | |
|-----------------|---|
| End point title | Percentage of participants with seroprotection measured by HI antibody response for each homologous and heterologous strain |
|-----------------|---|

End point description:

The percentage of participants in a given treatment group attaining a reciprocal HI titer of ≥ 40 on Day 21 (the percentage of vaccine recipients with a serum HI titer of at least 1:40 following vaccination) was measured using an HI assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. IPP set.

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

End point timeframe:
Baseline (Day 0), Day 21

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|--|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Homologous Strain (H1N1): Day 0 | 57.3 (50.2 to 64.1) | 52.8 (45.6 to 59.9) | | |
| Homologous Strain (H1N1): Day 21 | 77.2 (70.8 to 82.7) | 87.9 (82.6 to 92.1) | | |
| Homologous Strain (H3N2): Day 0 | 48.5 (41.5 to 55.6) | 52.8 (45.6 to 59.9) | | |
| Homologous Strain (H3N2): Day 21 | 72.3 (65.7 to 78.3) | 78.4 (72.0 to 83.9) | | |
| Homologous Strain (B/Colorado): Day 0 | 28.6 (22.6 to 35.3) | 22.1 (16.5 to 28.5) | | |
| Homologous Strain (B/Colorado): Day 21 | 40.3 (33.5 to 47.3) | 62.3 (55.2 to 69.1) | | |
| Homologous Strain (B/Phuket): Day 0 | 46.6 (39.6 to 53.7) | 38.7 (31.9 to 45.8) | | |
| Homologous Strain (B/Phuket): Day 21 | 64.1 (57.1 to 70.6) | 79.4 (73.1 to 84.8) | | |
| Heterologous Strain (H1N1): Day 0 | 21.8 (16.4 to 28.1) | 18.1 (13.0 to 24.2) | | |
| Heterologous Strain (H1N1): Day 21 | 22.8 (17.3 to 29.2) | 49.2 (42.1 to 56.4) | | |
| Heterologous Strain (H3N2): Day 0 | 35.4 (28.9 to 42.4) | 40.2 (33.3 to 47.4) | | |
| Heterologous Strain (H3N2): Day 21 | 50.0 (43.0 to 57.0) | 63.8 (56.7 to 70.5) | | |
| Heterologous Strain (B/Malaysia): Day 0 | 22.8 (17.3 to 29.2) | 17.6 (12.6 to 23.6) | | |
| Heterologous Strain (B/Malaysia): Day 21 | 30.1 (23.9 to 36.9) | 53.8 (46.6 to 60.8) | | |
| Heterologous Strain (B/Florida): Day 0 | 37.4 (30.8 to 44.4) | 31.2 (24.8 to 38.1) | | |
| Heterologous Strain (B/Florida): Day 21 | 58.7 (51.7 to 65.5) | 76.9 (70.4 to 82.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean fold rise (GMFR) of HI antibody response for each homologous and heterologous strain

| | |
|-----------------|---|
| End point title | Geometric mean fold rise (GMFR) of HI antibody response for each homologous and heterologous strain |
|-----------------|---|

End point description:

GMFR, the geometric mean of the ratio of GMTs (Day 21/Day 0), was measured using an HI assay

homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013, and the heterologous strains: H1N1 = A/Brisbane/59/2007; H3N2 = A/Uruguay/716/2007; B/Malaysia = B/Malaysia/2506/2004; B/Florida = B/Florida/4/2006. IPP set.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 0), Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|--|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Homologous Strain (H1N1) | 2.1 (1.8 to 2.4) | 3.9 (3.4 to 4.5) | | |
| Homologous Strain (H3N2) | 2.6 (2.2 to 3.0) | 2.9 (2.5 to 3.4) | | |
| Homologous Strain (B/Colorado) | 1.5 (1.3 to 1.8) | 3.8 (3.3 to 4.4) | | |
| Homologous Strain (B/Phuket) | 1.9 (1.6 to 2.1) | 3.3 (2.9 to 3.8) | | |
| Heterologous Strain (H1N1) | 1.1 (1.0 to 1.2) | 2.4 (2.2 to 2.6) | | |
| Heterologous Strain (H3N2) | 1.6 (1.5 to 1.8) | 2.1 (1.9 to 2.3) | | |
| Heterologous Strain (B/Malaysia) | 1.3 (1.1 to 1.4) | 3.0 (2.7 to 3.4) | | |
| Heterologous Strain (B/Florida) | 1.7 (1.5 to 1.9) | 3.4 (3.0 to 3.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Microneutralization (MN) antibody response for each homologous strain

| | |
|-----------------|---|
| End point title | GMTs of Microneutralization (MN) antibody response for each homologous strain |
|-----------------|---|

End point description:

GMTs were measured using an MN assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 0), Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|---|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1: Day 0 | 501.4 (420.6 to 597.8) | 511.2 (427.5 to 611.3) | | |
| H1N1: Day 21 | 1120.7 (926.3 to 1355.9) | 1807.0 (1488.6 to 2193.6) | | |
| H3N2: Day 0 | 227.4 (194.9 to 265.3) | 240.1 (205.3 to 280.8) | | |
| H3N2: Day 21 | 558.5 (461.2 to 676.3) | 437.0 (359.7 to 531.0) | | |
| B/Colorado: Day 0 | 62.7 (54.1 to 72.6) | 55.1 (47.5 to 64.0) | | |
| B/Colorado: Day 21 | 124.1 (105.4 to 146.2) | 193.1 (163.5 to 228.1) | | |
| B/Phuket: Day 0 | 50.5 (44.4 to 57.6) | 45.8 (40.1 to 52.3) | | |
| B/Phuket: Day 21 | 98.2 (85.7 to 112.6) | 143.4 (143.4 to 164.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with seroconversion measured by MN antibody response for each homologous strain

| | |
|---|--|
| End point title | Percentage of participants with seroconversion measured by MN antibody response for each homologous strain |
| End point description: | |
| The percentage of participants in a given treatment group with either a ≥ 4 -fold increase in reciprocal MN titers between Day 0 and Day 21 or a rise of undetectable MN titer (i.e. 7.1) pre-vaccination (Day 0) to an MN titer of ≥ 28.3 at Day 21 post-vaccination were measured using an MN assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 0 (pre-vaccination) to Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------------|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| H1N1 | 25.7 (19.9 to 32.3) | 43.2 (36.2 to 50.4) | | |

| | | | | |
|------------|---------------------|---------------------|--|--|
| H3N2 | 36.4 (29.8 to 43.4) | 26.6 (20.6 to 33.3) | | |
| B/Colorado | 19.9 (14.7 to 26.0) | 43.7 (36.7 to 50.9) | | |
| B/Phuket | 19.4 (14.2 to 25.5) | 41.2 (34.3 to 48.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR of MN antibody response for each homologous strain

| | |
|--|---|
| End point title | GMFR of MN antibody response for each homologous strain |
| End point description: | |
| GMFR, the geometric mean of the ratio of GMTs (Day 21/Day 0), was measured using an MN assay for H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 0), Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|--|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1 | 2.2 (1.9 to 2.6) | 3.5 (3.0 to 4.1) | | |
| H3N2 | 2.4 (2.1 to 2.8) | 1.8 (1.6 to 2.1) | | |
| B/Colorado | 2.0 (1.8 to 2.3) | 3.4 (3.0 to 3.9) | | |
| B/Phuket | 2.0 (1.8 to 2.2) | 3.1 (2.8 to 3.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Areas (GMA) of Single Radial Hemolysis (SRH) antibody response for each homologous strain

| | |
|---|--|
| End point title | Geometric Mean Areas (GMA) of Single Radial Hemolysis (SRH) antibody response for each homologous strain |
| End point description: | |
| GMA was measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set. | |
| End point type | Secondary |

End point timeframe:
Baseline (Day 0), Day 21

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|---|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: mm ² | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1: Day 0 | 23.8 (20.4 to 27.7) | 20.7 (17.7 to 24.2) | | |
| H1N1: Day 21 | 38.7 (34.7 to 43.1) | 48.9 (43.8 to 54.6) | | |
| H3N2: Day 0 | 6.3 (5.1 to 7.9) | 5.1 (4.1 to 6.3) | | |
| H3N2: Day 21 | 21.9 (17.2 to 28.0) | 13.2 (10.3 to 17.0) | | |
| B/Colorado: Day 0 | 33.7 (28.1 to 40.3) | 29.2 (24.3 to 35.1) | | |
| B/Colorado: Day 21 | 54.1 (47.3 to 61.8) | 61.0 (53.3 to 69.9) | | |
| B/Phuket: Day 0 | 21.5 (17.7 to 26.0) | 20.4 (16.8 to 24.8) | | |
| B/Phuket: Day 21 | 38.8 (33.5 to 44.9) | 50.2 (43.3 to 58.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with seroconversion measured by SRH antibody response for each homologous strain

| | |
|--|---|
| End point title | Percentage of participants with seroconversion measured by SRH antibody response for each homologous strain |
| End point description: The percentage of participants in a given treatment group showing at least 50 % increase in GMA between Days 0 and 21 were measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set. | |
| End point type | Secondary |
| End point timeframe: Day 0 (pre-vaccination) to Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------------|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| H1N1 | 34.0 (27.5 to 40.9) | 55.3 (48.1 to 62.3) | | |
| H3N2 | 45.1 (38.2 to 52.2) | 34.7 (28.1 to 41.7) | | |
| B/Colorado | 32.0 (25.7 to 38.9) | 49.7 (42.6 to 56.9) | | |
| B/Phuket | 35.9 (29.4 to 42.9) | 52.3 (45.1 to 59.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with seroprotection measured by SRH antibody response for each homologous strain

| | |
|---|---|
| End point title | Percentage of participants with seroprotection measured by SRH antibody response for each homologous strain |
| End point description: The percentage of participants in a given treatment group attaining an area ≥ 25 mm ² following vaccination (Day 21) were measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set. | |
| End point type | Secondary |
| End point timeframe: Baseline (Day 0), Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|-----------------------------------|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| H1N1: Day 0 | 56.8 (49.7 to 63.7) | 51.8 (44.6 to 58.9) | | |
| H1N1: Day 21 | 77.7 (71.4 to 83.2) | 89.4 (84.3 to 93.3) | | |
| H3N2: Day 0 | 27.7 (21.7 to 34.3) | 23.6 (17.9 to 30.1) | | |
| H3N2: Day 21 | 63.6 (56.6 to 70.2) | 51.8 (44.6 to 58.9) | | |
| B/Colorado: Day 0 | 71.8 (65.2 to 77.9) | 69.8 (63.0 to 76.1) | | |
| B/Colorado: Day 21 | 87.9 (82.6 to 92.0) | 89.4 (84.3 to 93.3) | | |

| | | | | |
|------------------|---------------------|---------------------|--|--|
| B/Phuket: Day 0 | 63.6 (56.6 to 70.2) | 60.8 (53.7 to 67.6) | | |
| B/Phuket: Day 21 | 76.2 (69.8 to 81.9) | 87.9 (82.6 to 92.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: GMFR of SRH antibody response for each homologous strain

| | |
|---|--|
| End point title | GMFR of SRH antibody response for each homologous strain |
| End point description: GMFR, the geometric mean of the ratio of GMTs (Day 21/Day 0), was measured using an SRH assay for homologous strains: H1N1 = A/Michigan/45/2015; H3N2 = A/Singapore/INFIMH-16-0019/2016; B/Colorado = B/Colorado/06/2017; B/Phuket = B/Phuket/3073/2013. IPP set. | |
| End point type | Secondary |
| End point timeframe: Baseline (Day 0), Day 21 | |

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|--|----------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 199 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1 | 1.7 (1.6 to 1.8) | 2.3 (2.1 to 2.5) | | |
| H3N2 | 3.6 (2.9 to 4.4) | 2.5 (2.0 to 3.1) | | |
| B/Colorado | 1.7 (1.5 to 1.9) | 2.0 (1.8 to 2.2) | | |
| B/Phuket | 1.8 (1.6 to 2.1) | 2.4 (2.2 to 2.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with at least one solicited local and systemic reactions

| | |
|---|---|
| End point title | Number of participants with at least one solicited local and systemic reactions |
| End point description: Participants were monitored for both solicited local reactions (erythema, swelling, and pain at the injection site) and solicited systemic reactions (fever, headache, fatigue, muscle aches, joint aches, chills, a feeling of general discomfort, swelling in the axilla, and swelling in the neck) from the time of vaccination through Day 7. Any solicited local or systemic immediate complaint was also included. SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis. | |
| End point type | Secondary |

End point timeframe:

Day 0 (post-vaccination) to Day 7

| End point values | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | | |
|------------------------------|--|-----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6352 | 6366 | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Solicited Local Reactions | 1954 | 1460 | | |
| Solicited Systemic Reactions | 1682 | 1497 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 0 (post-vaccination) up to ~9 months

Adverse event reporting additional description:

SAS. Participants that were non-compliant to protocol/GCP, as per investigator, were excluded from analysis.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------------------|
| Reporting group title | Quadrivalent (30 µg) VLP Vaccine |
|-----------------------|----------------------------------|

Reporting group description:

Participants received one IM injection of 0.5 mL of 30 µg/strain of the Quadrivalent VLP Influenza Vaccine on Day 0.

| | |
|-----------------------|-----------------------------|
| Reporting group title | Active Comparator (Fluarix) |
|-----------------------|-----------------------------|

Reporting group description:

Participants received one IM injection of 0.5 mL of 15 µg/strain of the Fluarix Quadrivalent® comparator vaccine on Day 0.

| Serious adverse events | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | |
|---|----------------------------------|-----------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 263 / 6352 (4.14%) | 266 / 6366 (4.18%) | |
| number of deaths (all causes) | 12 | 17 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acral lentiginous melanoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign neoplasm of bladder | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary neoplasm | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder cancer | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 5 / 6366 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial neoplasm | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic lymphocytic leukaemia | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon adenoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial cancer stage I | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Female reproductive neoplasm | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cancer metastatic | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraductal papillary mucinous neoplasm | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal cancer | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung squamous cell carcinoma stage III | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoplasmacytoid lymphoma/immunocytoma recurrent | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma stage II | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mesothelioma | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic malignant melanoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Neoplasm malignant | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parathyroid tumour benign | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 6 / 6366 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer metastatic | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal cancer | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal neoplasm | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Throat cancer | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid cancer recurrent | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsil cancer | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Triple negative breast cancer | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Waldenstrom's macroglobulinaemia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Accelerated hypertension | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angiodysplasia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic dissection | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic stenosis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Circulatory collapse | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extremity necrosis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral arterial occlusive disease | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral vascular disorder | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicose vein | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Atrial appendage closure | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 4 / 6366 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Incarcerated hernia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical failure | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular stent stenosis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Endometriosis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectocele | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine prolapse | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterovaginal prolapse | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaginal prolapse | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicocele | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|------------------|------------------|--|
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchospasm | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 6 / 6366 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Emphysema | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 6 / 6366 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic idiopathic pain syndrome | | | |

| | | | |
|--|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Completed suicide | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disorientation | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mood disorder due to a general medical condition | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device dislocation | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stenosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cirrhosis | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sphincter of Oddi dysfunction | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Fibrin D dimer increased | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Acetabulum fracture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Animal attack | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 4 / 6366 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical vertebral fracture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Concussion | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|------------------|------------------|--|
| Contusion | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Fascial rupture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body aspiration | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fractured coccyx | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fractured sacrum | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lacrimal structure injury | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb injury | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus injury | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative ileus | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pubis fracture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendon rupture | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention postoperative | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hamartoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syringomyelia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 6 / 6352 (0.09%) | 8 / 6366 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arrhythmia | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Arteriosclerosis coronary artery | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 11 / 6352 (0.17%) | 12 / 6366 (0.19%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardio-respiratory arrest | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery occlusion | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Sinus arrest | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachyarrhythmia | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar stroke | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 7 / 6352 (0.11%) | 9 / 6366 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Chronic inflammatory demyelinating polyradiculoneuropathy | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia Alzheimer's type | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| IVth nerve paralysis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parkinsonism | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parkinson's disease | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylitic myelopathy | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 5 / 6366 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient global amnesia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 6 / 6352 (0.09%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebrobasilar insufficiency | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic anaemia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Microcytic anaemia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic haematoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo positional | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vestibular disorder | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |

| | | | |
|---|------------------|------------------|--|
| Amaurosis fugax | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Corneal degeneration | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dacryostenosis acquired | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Colitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer perforation | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus hernia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated inguinal hernia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mesenteric arterial occlusion | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Portal hypertensive gastropathy | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctitis ulcerative | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reactive gastropathy | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder prolapse | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Back pain | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Camptocormia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Exostosis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lateral patellar compression syndrome | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 9 / 6352 (0.14%) | 9 / 6366 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polymyalgia rheumatica | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal column stenosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal osteoarthritis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylolisthesis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial cyst | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic scleroderma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 4 / 6366 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis infective | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Empyema | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocarditis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis Escherichia coli | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| H1N1 influenza | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 4 / 6366 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising fasciitis staphylococcal | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis bacterial | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngeal abscess | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 20 / 6352 (0.31%) | 11 / 6366 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 20 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Pneumonia legionella | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gout | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Quadrivalent (30 µg) VLP Vaccine | Active Comparator (Fluarix) | |
|---|----------------------------------|-----------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 88 / 6352 (1.39%) | 138 / 6366 (2.17%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Benign neoplasm of thyroid gland | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Breast cancer stage I | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Chronic lymphocytic leukaemia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye naevus | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Haemangioma of liver | | | |

| | | | |
|---|-----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Malignant melanoma subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Squamous cell carcinoma subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 5 | 0 / 6366 (0.00%) 0 | |
| Squamous cell carcinoma of skin subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Vascular disorders | | | |
| Aneurysm subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Aortic arteriosclerosis subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 3 / 6366 (0.05%) 3 | |
| Aortic dilatation subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Aortic disorder subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Aortic stenosis subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 0 / 6366 (0.00%) 0 | |
| Deep vein thrombosis subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Flushing subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 3 / 6366 (0.05%) 4 | |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 | |

| | | | |
|--|-------------------|-------------------|--|
| Hot flush | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hypertension | | | |
| subjects affected / exposed | 35 / 6352 (0.55%) | 27 / 6366 (0.42%) | |
| occurrences (all) | 35 | 27 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 0 | 2 | |
| Microangiopathy | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Peripheral coldness | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Peripheral vascular disorder | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Thrombosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Varicose vein | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Axillary pain | | | |

| | | |
|---------------------------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Chest discomfort | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Chest pain | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 5 / 6366 (0.08%) |
| occurrences (all) | 3 | 5 |
| Chills | | |
| subjects affected / exposed | 15 / 6352 (0.24%) | 15 / 6366 (0.24%) |
| occurrences (all) | 15 | 15 |
| Discomfort | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 2 |
| Face oedema | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Facial pain | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Fatigue | | |
| subjects affected / exposed | 26 / 6352 (0.41%) | 32 / 6366 (0.50%) |
| occurrences (all) | 27 | 35 |
| Feeling hot | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Gait disturbance | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| General physical health deterioration | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hypothermia | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Induration | | |

| | | |
|----------------------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Inflammation | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Influenza like illness | | |
| subjects affected / exposed | 8 / 6352 (0.13%) | 11 / 6366 (0.17%) |
| occurrences (all) | 8 | 11 |
| Injected limb mobility decreased | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Injection site bruising | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 4 / 6366 (0.06%) |
| occurrences (all) | 2 | 4 |
| Injection site erythema | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 3 / 6366 (0.05%) |
| occurrences (all) | 2 | 3 |
| Injection site haematoma | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Injection site induration | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Injection site pain | | |
| subjects affected / exposed | 12 / 6352 (0.19%) | 7 / 6366 (0.11%) |
| occurrences (all) | 12 | 7 |
| Injection site pruritus | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 4 / 6366 (0.06%) |
| occurrences (all) | 3 | 4 |
| Injection site reaction | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Injection site swelling | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 5 / 6366 (0.08%) |
| occurrences (all) | 3 | 5 |
| Injection site warmth | | |

| | | |
|--------------------------------|-------------------|-------------------|
| subjects affected / exposed | 4 / 6352 (0.06%) | 2 / 6366 (0.03%) |
| occurrences (all) | 4 | 2 |
| Malaise | | |
| subjects affected / exposed | 11 / 6352 (0.17%) | 6 / 6366 (0.09%) |
| occurrences (all) | 11 | 6 |
| Mass | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Oedema peripheral | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) |
| occurrences (all) | 1 | 3 |
| Pain | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 2 / 6366 (0.03%) |
| occurrences (all) | 4 | 2 |
| Peripheral swelling | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Pyrexia | | |
| subjects affected / exposed | 9 / 6352 (0.14%) | 15 / 6366 (0.24%) |
| occurrences (all) | 9 | 16 |
| Swelling | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 6 / 6366 (0.09%) |
| occurrences (all) | 5 | 6 |
| Tenderness | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Vaccination site haematoma | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Vaccination site hypoaesthesia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Vaccination site induration | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Vaccination site pain | | |

| | | | |
|--|-----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Vaccination site pruritus subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Immune system disorders | | | |
| Drug hypersensitivity subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Seasonal allergy subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 3 / 6366 (0.05%) 3 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia subjects affected / exposed occurrences (all) | 4 / 6352 (0.06%) 4 | 7 / 6366 (0.11%) 7 | |
| Erectile dysfunction subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Ovarian cyst subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Prostatomegaly subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Vulvovaginal pruritus subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Allergic cough subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Asthma subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 0 / 6366 (0.00%) 0 | |
| Atelectasis | | | |

| | | |
|---------------------------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Chronic obstructive pulmonary disease | | |
| subjects affected / exposed | 8 / 6352 (0.13%) | 5 / 6366 (0.08%) |
| occurrences (all) | 8 | 5 |
| Cough | | |
| subjects affected / exposed | 42 / 6352 (0.66%) | 46 / 6366 (0.72%) |
| occurrences (all) | 42 | 47 |
| Dry throat | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dysphonia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Dyspnoea | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 7 / 6366 (0.11%) |
| occurrences (all) | 4 | 7 |
| Dyspnoea exertional | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Emphysema | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 2 / 6366 (0.03%) |
| occurrences (all) | 3 | 2 |
| Epistaxis | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 1 / 6366 (0.02%) |
| occurrences (all) | 4 | 1 |
| Nasal congestion | | |
| subjects affected / exposed | 29 / 6352 (0.46%) | 30 / 6366 (0.47%) |
| occurrences (all) | 31 | 32 |
| Nasal discomfort | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Oropharyngeal pain | | |
| subjects affected / exposed | 47 / 6352 (0.74%) | 41 / 6366 (0.64%) |
| occurrences (all) | 47 | 42 |

| | | |
|------------------------------|-------------------|-------------------|
| Pharyngeal oedema | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pharyngeal paraesthesia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Productive cough | | |
| subjects affected / exposed | 10 / 6352 (0.16%) | 21 / 6366 (0.33%) |
| occurrences (all) | 10 | 22 |
| Pulmonary hypertension | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 3 / 6366 (0.05%) |
| occurrences (all) | 2 | 3 |
| Pulmonary mass | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Pulmonary oedema | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Respiratory disorder | | |
| subjects affected / exposed | 16 / 6352 (0.25%) | 17 / 6366 (0.27%) |
| occurrences (all) | 16 | 17 |
| Respiratory symptom | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Respiratory tract congestion | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 0 / 6366 (0.00%) |
| occurrences (all) | 4 | 0 |
| Rhinitis allergic | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 3 / 6366 (0.05%) |
| occurrences (all) | 0 | 3 |
| Rhinorrhoea | | |
| subjects affected / exposed | 41 / 6352 (0.65%) | 56 / 6366 (0.88%) |
| occurrences (all) | 42 | 56 |
| Sinus congestion | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |

| | | | |
|------------------------------------|-------------------|-------------------|--|
| Sinus pain | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 1 | 2 | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 2 | 1 | |
| Sneezing | | | |
| subjects affected / exposed | 31 / 6352 (0.49%) | 25 / 6366 (0.39%) | |
| occurrences (all) | 33 | 27 | |
| Throat irritation | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 2 | 2 | |
| Throat tightness | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tonsillar cyst | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Upper respiratory tract congestion | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Wheezing | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 4 | 1 | |
| Psychiatric disorders | | | |
| Abnormal dreams | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Aggression | | | |

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|-----------------------------|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Anxiety | | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 5 | 1 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Fear | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Initial insomnia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 4 | 2 | |
| Listless | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Nervousness | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Restlessness | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 2 | |
| Sleep disorder | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Investigations | | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 3 / 6366 (0.05%) | |
| occurrences (all) | 0 | 3 | |

| | | | |
|---|-------------------------|-----------------------|--|
| Blood pressure increased subjects affected / exposed occurrences (all) | 13 / 6352 (0.20%) 13 | 9 / 6366 (0.14%) 9 | |
| Blood thyroid stimulating hormone increased subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Body temperature increased subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 | |
| Cardiac imaging procedure abnormal subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Hepatic enzyme increased subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Thyroid hormones decreased subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Injury, poisoning and procedural complications | | | |
| Anaemia postoperative subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Animal bite subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Arthropod bite subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 4 / 6366 (0.06%) 4 | |
| Arthropod sting subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Back injury subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Chest injury | | | |

| | | |
|-----------------------------|------------------|------------------|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Contusion | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 3 |
| Epicondylitis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eye injury | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Face injury | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Facial bones fracture | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Fall | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 7 / 6366 (0.11%) |
| occurrences (all) | 1 | 7 |
| Head injury | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Joint injury | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Laceration | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 4 / 6366 (0.06%) |
| occurrences (all) | 3 | 4 |
| Ligament sprain | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) |
| occurrences (all) | 3 | 0 |
| Limb injury | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Meniscus injury | | |

| | | |
|-----------------------------|------------------|------------------|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Muscle contusion | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Muscle rupture | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Muscle strain | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 3 / 6366 (0.05%) |
| occurrences (all) | 5 | 3 |
| Post-traumatic pain | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Procedural pain | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 5 / 6366 (0.08%) |
| occurrences (all) | 3 | 6 |
| Pubis fracture | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Rib fracture | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Scratch | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Skin abrasion | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 3 / 6366 (0.05%) |
| occurrences (all) | 0 | 3 |
| Spinal compression fracture | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Sunburn | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Synovial rupture | | |

| | | | |
|---|-----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Tendon rupture subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 3 | 0 / 6366 (0.00%) 0 | |
| Tibia fracture subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Tongue injury subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Toxicity to various agents subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Wound subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Wound complication subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Wrist fracture subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Bone contusion subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Cardiac disorders Acute left ventricular failure subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Angina pectoris subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Aortic valve incompetence subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |

| | | |
|----------------------------------|-------------------|-------------------|
| Aortic valve stenosis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Arrhythmia | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 2 |
| Arteriosclerosis coronary artery | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Atrial fibrillation | | |
| subjects affected / exposed | 11 / 6352 (0.17%) | 11 / 6366 (0.17%) |
| occurrences (all) | 11 | 11 |
| Atrial flutter | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Bradycardia | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) |
| occurrences (all) | 3 | 0 |
| Bundle branch block bilateral | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cardiac dysfunction | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Cardiac failure congestive | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Cardiomegaly | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Cardiomyopathy | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Cardiovascular disorder | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |

| | | |
|--|-----------------------|-----------------------|
| Coronary artery disease subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 5 / 6366 (0.08%) 5 |
| Coronary artery stenosis subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 |
| Dilatation atrial subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 |
| Extrasystoles subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 |
| Hypertensive heart disease subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 |
| Left atrial dilatation subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 |
| Left ventricular dysfunction subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 |
| Left ventricular hypertrophy subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 5 / 6366 (0.08%) 5 |
| Mitral valve calcification subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 |
| Mitral valve incompetence subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 4 / 6366 (0.06%) 4 |
| Palpitations subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 |
| Pulmonary valve incompetence subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 |

| | | | |
|--|-----------------------|-----------------------|--|
| Right atrial dilatation subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Sinus node dysfunction subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Tachycardia subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Tricuspid valve incompetence subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 5 / 6366 (0.08%) 5 | |
| Nervous system disorders | | | |
| Carotid artery stenosis subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 1 / 6366 (0.02%) 1 | |
| Carpal tunnel syndrome subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Cerebral atrophy subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 3 / 6366 (0.05%) 3 | |
| Cerebral microangiopathy subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Complex regional pain syndrome subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Dementia subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Dementia Alzheimer's type subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Dizziness | | | |

| | | |
|-----------------------------|-------------------|-------------------|
| subjects affected / exposed | 19 / 6352 (0.30%) | 24 / 6366 (0.38%) |
| occurrences (all) | 20 | 25 |
| Dysgeusia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Facial paralysis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Head discomfort | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Headache | | |
| subjects affected / exposed | 61 / 6352 (0.96%) | 66 / 6366 (1.04%) |
| occurrences (all) | 73 | 71 |
| Hypoaesthesia | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |
| Hypogeusia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Memory impairment | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Migraine | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 3 / 6366 (0.05%) |
| occurrences (all) | 2 | 3 |
| Movement disorder | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Myasthenia gravis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Neuralgia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Neuropathy peripheral | | |

| | | |
|-----------------------------|------------------|------------------|
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 3 |
| Paraesthesia | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) |
| occurrences (all) | 3 | 0 |
| Parkinson's disease | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Polyneuropathy | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Posterior cortical atrophy | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Presyncope | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Radiculopathy | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Restless legs syndrome | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 3 / 6366 (0.05%) |
| occurrences (all) | 2 | 3 |
| Sciatica | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 2 |
| Sinus headache | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 2 |
| Somnolence | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Syncope | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Tension headache | | |

| | | | |
|--|-----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 0 / 6366 (0.00%) 0 | |
| Trigeminal neuralgia subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Vith nerve paralysis subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Visual field defect subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 3 | |
| White matter lesion subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 2 / 6366 (0.03%) 2 | |
| Increased tendency to bruise subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Iron deficiency anemia subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Lymph node pain subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 0 / 6366 (0.00%) 0 | |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 1 / 6366 (0.02%) 1 | |
| Ear and labyrinth disorders | | | |
| Cerumen impaction subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 0 / 6366 (0.00%) 0 | |
| Ear discomfort | | | |

| | | | |
|---------------------------------|------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Ear pain | | | |
| subjects affected / exposed | 7 / 6352 (0.11%) | 7 / 6366 (0.11%) | |
| occurrences (all) | 7 | 7 | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vertigo | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 4 / 6366 (0.06%) | |
| occurrences (all) | 3 | 4 | |
| Vertigo positional | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Astigmatism | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 0 | 2 | |
| Binocular eye movement disorder | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Blepharochalasis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Blindness transient | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cataract | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Chalazion | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |

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| Conjunctival haemorrhage | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Corneal warpage | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dry age-related macular degeneration | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Dry eye | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |
| Eye discharge | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eye haemorrhage | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eye inflammation | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eye irritation | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Eye pain | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eye pruritus | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Eye swelling | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Eyelid irritation | | |

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|--|------------------|------------------|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eyelid margin crusting | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eyelid oedema | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Eyelid pain | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Glaucoma | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |
| Hyalosis asteroid | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Keratitis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Lacrimation increased | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Macular degeneration | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Macular fibrosis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Neovascular age-related macular degeneration | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Ocular hyperaemia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |

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|--|-----------------------|------------------------|--|
| Ocular rosacea subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Vision blurred subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Visual impairment subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Vitreous haemorrhage subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 0 / 6366 (0.00%) 0 | |
| Abdominal distension subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 1 / 6366 (0.02%) 1 | |
| Abdominal hernia subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 1 / 6366 (0.02%) 1 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 8 / 6352 (0.13%) 8 | 7 / 6366 (0.11%) 7 | |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 8 / 6366 (0.13%) 10 | |
| Anal incontinence subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Aphthous ulcer | | | |

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|-----------------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Barrett's oesophagus | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Cheilitis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Chronic gastritis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Constipation | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 6 / 6366 (0.09%) |
| occurrences (all) | 4 | 6 |
| Diarrhoea | | |
| subjects affected / exposed | 50 / 6352 (0.79%) | 53 / 6366 (0.83%) |
| occurrences (all) | 53 | 56 |
| Diverticulum | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) |
| occurrences (all) | 1 | 3 |
| Diverticulum intestinal | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Dry mouth | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dyspepsia | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 3 / 6366 (0.05%) |
| occurrences (all) | 2 | 3 |
| Dysphagia | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Enlarged uvula | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Faeces soft | | |

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| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Flatulence | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Food poisoning | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Gastric ulcer | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Gastritis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Gastrooesophageal reflux disease | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 5 / 6366 (0.08%) |
| occurrences (all) | 3 | 5 |
| Haemorrhoidal haemorrhage | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Haemorrhoids | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hiatus hernia | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 2 |
| Irritable bowel syndrome | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Large intestine polyp | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Lip erythema | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 2 |
| Lip pruritus | | |

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| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 2 |
| Lip swelling | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lip ulceration | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Malocclusion | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Nausea | | |
| subjects affected / exposed | 27 / 6352 (0.43%) | 30 / 6366 (0.47%) |
| occurrences (all) | 27 | 32 |
| Oesophageal food impaction | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Oesophageal motility disorder | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Oesophagitis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Oral pruritus | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Palatal oedema | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Rectal haemorrhage | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Salivary gland calculus | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Swollen tongue | | |

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| subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Tongue blistering subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Tooth impacted subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Tooth loss subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 0 / 6366 (0.00%) 0 | |
| Toothache subjects affected / exposed occurrences (all) | 8 / 6352 (0.13%) 8 | 6 / 6366 (0.09%) 6 | |
| Vomiting subjects affected / exposed occurrences (all) | 13 / 6352 (0.20%) 13 | 13 / 6366 (0.20%) 14 | |
| Hepatobiliary disorders | | | |
| Biliary colic subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 0 / 6366 (0.00%) 0 | |
| Cholangitis subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Cholangitis acute subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Cholecystitis acute subjects affected / exposed occurrences (all) | 1 / 6352 (0.02%) 1 | 0 / 6366 (0.00%) 0 | |
| Hepatic cirrhosis subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Hepatic steatosis subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 | |

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| Portal vein thrombosis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Steatohepatitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood blister | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 1 | 2 | |
| Dermatitis contact | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 2 | 2 | |
| Diabetic foot | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Eczema | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 3 / 6366 (0.05%) | |
| occurrences (all) | 3 | 3 | |
| Erythema | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 5 / 6366 (0.08%) | |
| occurrences (all) | 1 | 5 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Ingrowing nail | | | |

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| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Ingrown hair | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Nail bed disorder | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Night sweats | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Pruritus | | |
| subjects affected / exposed | 9 / 6352 (0.14%) | 8 / 6366 (0.13%) |
| occurrences (all) | 10 | 9 |
| Pruritus generalised | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 3 / 6366 (0.05%) |
| occurrences (all) | 3 | 4 |
| Rash | | |
| subjects affected / exposed | 12 / 6352 (0.19%) | 8 / 6366 (0.13%) |
| occurrences (all) | 12 | 8 |
| Rash generalised | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Skin discolouration | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Skin ulcer | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Stasis dermatitis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Urticaria | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 2 |
| Renal and urinary disorders | | |

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| Acute kidney injury | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Bladder discomfort | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Calculus urinary | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Chronic kidney disease | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 4 / 6366 (0.06%) |
| occurrences (all) | 3 | 4 |
| Hypertensive nephropathy | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hypertonic bladder | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Micturition urgency | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Nephrolithiasis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Nephrotic syndrome | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pollakiuria | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 3 / 6366 (0.05%) |
| occurrences (all) | 0 | 3 |
| Renal cyst | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Renal disorder | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |

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| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Urinary tract obstruction subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Lower urinary tract symptoms subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Endocrine disorders Goitre subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 2 / 6366 (0.03%) 2 | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 2 / 6352 (0.03%) 2 | 1 / 6366 (0.02%) 1 | |
| Hypothyroidism subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 4 / 6366 (0.06%) 4 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 25 / 6352 (0.39%) 25 | 30 / 6366 (0.47%) 30 | |
| Arthritis subjects affected / exposed occurrences (all) | 4 / 6352 (0.06%) 4 | 1 / 6366 (0.02%) 1 | |
| Back pain subjects affected / exposed occurrences (all) | 20 / 6352 (0.31%) 21 | 26 / 6366 (0.41%) 27 | |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 6352 (0.00%) 0 | 1 / 6366 (0.02%) 1 | |
| Bursitis subjects affected / exposed occurrences (all) | 3 / 6352 (0.05%) 3 | 3 / 6366 (0.05%) 3 | |
| Coccydynia | | | |

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|----------------------------------|------------------|------------------|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dupuytren's contracture | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Facet joint syndrome | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Flank pain | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Groin pain | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Intervertebral disc degeneration | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Intervertebral disc protrusion | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) |
| occurrences (all) | 3 | 0 |
| Joint swelling | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Limb discomfort | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |
| Lumbar spinal stenosis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Muscle spasms | | |
| subjects affected / exposed | 9 / 6352 (0.14%) | 3 / 6366 (0.05%) |
| occurrences (all) | 9 | 3 |
| Muscle tightness | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 1 / 6366 (0.02%) |
| occurrences (all) | 3 | 1 |
| Muscular weakness | | |

| | | |
|-----------------------------|-------------------|-------------------|
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Musculoskeletal chest pain | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) |
| occurrences (all) | 1 | 3 |
| Musculoskeletal pain | | |
| subjects affected / exposed | 11 / 6352 (0.17%) | 12 / 6366 (0.19%) |
| occurrences (all) | 11 | 12 |
| Musculoskeletal stiffness | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 5 / 6366 (0.08%) |
| occurrences (all) | 1 | 5 |
| Myalgia | | |
| subjects affected / exposed | 32 / 6352 (0.50%) | 35 / 6366 (0.55%) |
| occurrences (all) | 34 | 35 |
| Myosclerosis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Neck mass | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Neck pain | | |
| subjects affected / exposed | 10 / 6352 (0.16%) | 10 / 6366 (0.16%) |
| occurrences (all) | 11 | 10 |
| Nuchal rigidity | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Osteoarthritis | | |
| subjects affected / exposed | 7 / 6352 (0.11%) | 12 / 6366 (0.19%) |
| occurrences (all) | 7 | 12 |
| Osteopenia | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 2 / 6366 (0.03%) |
| occurrences (all) | 2 | 2 |
| Osteoporosis | | |
| subjects affected / exposed | 6 / 6352 (0.09%) | 4 / 6366 (0.06%) |
| occurrences (all) | 6 | 4 |
| Osteosclerosis | | |

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|-----------------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Pain in extremity | | |
| subjects affected / exposed | 14 / 6352 (0.22%) | 11 / 6366 (0.17%) |
| occurrences (all) | 14 | 11 |
| Periarthritis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Plantar fasciitis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Polyarthritis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Polymyalgia rheumatica | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rheumatoid arthritis | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |
| Rotator cuff syndrome | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Spinal column stenosis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Spinal osteoarthritis | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 1 / 6366 (0.02%) |
| occurrences (all) | 3 | 1 |
| Spondylitis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Spondylolisthesis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Synovial cyst | | |

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|----------------------------------|-------------------|------------------|--|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tendonitis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Torticollis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Vertebral foraminal stenosis | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Adenovirus infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Borrelia infection | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 12 / 6352 (0.19%) | 8 / 6366 (0.13%) | |
| occurrences (all) | 12 | 8 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) | |
| occurrences (all) | 1 | 3 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 3 / 6366 (0.05%) | |
| occurrences (all) | 2 | 3 | |
| Cystitis | | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 6 / 6366 (0.09%) | |
| occurrences (all) | 2 | 6 | |

| | | |
|----------------------------------|------------------|------------------|
| Cystitis escherichia | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Diverticulitis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Ear infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Erysipelas | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Eye infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Eye infection bacterial | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Folliculitis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Gastroenteritis | | |
| subjects affected / exposed | 6 / 6352 (0.09%) | 8 / 6366 (0.13%) |
| occurrences (all) | 6 | 8 |
| Gastroenteritis viral | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 1 / 6366 (0.02%) |
| occurrences (all) | 3 | 1 |
| Gastrointestinal infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Gastrointestinal viral infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Genital infection fungal | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |

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|--|------------------|-------------------|
| Gingivitis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Haemorrhagic fever with renal syndrome | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Helicobacter infection | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Hepatitis C | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Herpes simplex | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 3 / 6366 (0.05%) |
| occurrences (all) | 1 | 3 |
| Herpes zoster | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 5 / 6366 (0.08%) |
| occurrences (all) | 5 | 5 |
| Hordeolum | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Infected bite | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 2 / 6366 (0.03%) |
| occurrences (all) | 0 | 2 |
| Infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Influenza | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 13 / 6366 (0.20%) |
| occurrences (all) | 3 | 14 |
| Laryngitis | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Localised infection | | |

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|-----------------------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lower respiratory tract infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Nasal herpes | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Nasopharyngitis | | |
| subjects affected / exposed | 88 / 6352 (1.39%) | 76 / 6366 (1.19%) |
| occurrences (all) | 88 | 77 |
| Onychomycosis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 2 / 6366 (0.03%) |
| occurrences (all) | 1 | 2 |
| Oral candidiasis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Oral herpes | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 3 / 6366 (0.05%) |
| occurrences (all) | 5 | 3 |
| Otitis media | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Periodontitis | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |
| Pertussis | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Pharyngitis | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 0 / 6366 (0.00%) |
| occurrences (all) | 4 | 0 |
| Pilonidal cyst | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Pneumonia | | |

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|-----------------------------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 6352 (0.02%) | 4 / 6366 (0.06%) |
| occurrences (all) | 1 | 4 |
| Respiratory tract infection | | |
| subjects affected / exposed | 8 / 6352 (0.13%) | 5 / 6366 (0.08%) |
| occurrences (all) | 8 | 5 |
| Respiratory tract infection viral | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Rhinitis | | |
| subjects affected / exposed | 9 / 6352 (0.14%) | 6 / 6366 (0.09%) |
| occurrences (all) | 9 | 6 |
| Root canal infection | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Sinusitis | | |
| subjects affected / exposed | 13 / 6352 (0.20%) | 9 / 6366 (0.14%) |
| occurrences (all) | 13 | 9 |
| Sinusitis bacterial | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Streptococcal infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Tinea infection | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Tooth abscess | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Tooth infection | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 1 / 6366 (0.02%) |
| occurrences (all) | 2 | 1 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 52 / 6352 (0.82%) | 47 / 6366 (0.74%) |
| occurrences (all) | 53 | 48 |
| Urinary tract infection | | |

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|------------------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 15 / 6352 (0.24%) | 13 / 6366 (0.20%) | |
| occurrences (all) | 15 | 13 | |
| Vaginal infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Varicella zoster virus infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 0 / 6366 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Dyslipidaemia | | | |
| subjects affected / exposed | 3 / 6352 (0.05%) | 2 / 6366 (0.03%) | |
| occurrences (all) | 3 | 2 | |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |
| Gout | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 5 / 6366 (0.08%) | |
| occurrences (all) | 0 | 5 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 0 | 1 | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 8 / 6352 (0.13%) | 5 / 6366 (0.08%) | |
| occurrences (all) | 8 | 5 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) | |
| occurrences (all) | 1 | 1 | |

| | | |
|-----------------------------|------------------|------------------|
| Hyperlipidaemia | | |
| subjects affected / exposed | 5 / 6352 (0.08%) | 2 / 6366 (0.03%) |
| occurrences (all) | 5 | 2 |
| Hypoglycaemia | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 3 |
| Hypokalaemia | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Iron deficiency | | |
| subjects affected / exposed | 2 / 6352 (0.03%) | 0 / 6366 (0.00%) |
| occurrences (all) | 2 | 0 |
| Ketoacidosis | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 0 / 6366 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lactose intolerance | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Lipid metabolism disorder | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |
| Type 2 diabetes mellitus | | |
| subjects affected / exposed | 4 / 6352 (0.06%) | 8 / 6366 (0.13%) |
| occurrences (all) | 4 | 8 |
| Vitamin B12 deficiency | | |
| subjects affected / exposed | 0 / 6352 (0.00%) | 1 / 6366 (0.02%) |
| occurrences (all) | 0 | 1 |
| Vitamin D deficiency | | |
| subjects affected / exposed | 1 / 6352 (0.02%) | 1 / 6366 (0.02%) |
| occurrences (all) | 1 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 24 July 2018 | <p>The purpose of Amendment No. 01 was to add precision to Protocol version 1.1 around key elements of the protocol:</p> <ul style="list-style-type: none">• Clarification of the testing to be applied for primary, secondary, and exploratory outcomes;• Clarification of the rationale for comparator vaccine choice;• Clarification of the statistical analysis plan;• Specification of the needle length required for obese subjects (body mass index greater than 30 kg/m²). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported