



Clinical trial results:

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of Pulmaquin® in the Management of Chronic Lung Infections with Pseudomonas aeruginosa in Subjects with Non-Cystic Fibrosis Bronchiectasis, including 28 Day Open-Label Extension (ORBIT-4)

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2013-005366-19 |
| Trial protocol | GB HU IT ES RO PL FR |
| Global end of trial date | 12 October 2016 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 25 April 2018 |
| First version publication date | 25 April 2018 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | ARD-3150-1202 |
|-----------------------|---------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02104245 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Aradigm Corporation |
| Sponsor organisation address | 3929 Point Eden Way, Hayward, California, United States, 94545 |
| Public contact | Clinical Operations, Aradigm Corporation, +1 510 265 8895, JacksonA@aradigm.com |
| Scientific contact | Medical and Drug Development, Aradigm Corporation, +1 510 265 8838, froehlichj@aradigm.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 | 07 October 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 11 August 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 October 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the efficacy of Linhaliq compared to placebo in the management of chronic lung infections with *P. aeruginosa* in subjects with non-cystic fibrosis (non-CF) bronchiectasis by evaluating the time to first pulmonary exacerbation in the Double-Blind Phase.

Protection of trial subjects:

The study was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 28 May 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects**Subjects enrolled per country**

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Israel: 24 |
| Country: Number of subjects enrolled | New Zealand: 16 |
| Country: Number of subjects enrolled | Georgia: 28 |
| Country: Number of subjects enrolled | Serbia: 10 |
| Country: Number of subjects enrolled | Korea, Republic of: 14 |
| Country: Number of subjects enrolled | Poland: 9 |
| Country: Number of subjects enrolled | Romania: 17 |
| Country: Number of subjects enrolled | Spain: 22 |
| Country: Number of subjects enrolled | United Kingdom: 43 |
| Country: Number of subjects enrolled | France: 9 |
| Country: Number of subjects enrolled | Hungary: 9 |
| Country: Number of subjects enrolled | Italy: 10 |
| Country: Number of subjects enrolled | Australia: 26 |
| Country: Number of subjects enrolled | Peru: 21 |
| Country: Number of subjects enrolled | United States: 36 |
| Country: Number of subjects enrolled | Canada: 10 |
| Worldwide total number of subjects | 304 |
| EEA total number of subjects | 119 |

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) | 139 |
| From 65 to 84 years | 162 |
| 85 years and over | 3 |

Subject disposition

Recruitment

Recruitment details:

96 clinical sites screened at least one subject for the study. The sites were located in Australia, Canada, France, Georgia, Hungary, Israel, Italy, New Zealand, Peru, Poland, Romania, Serbia, South Korea, Spain, the United Kingdom, and the US. The first subject was screened on 28 May 2014, and the final subject screened on 04 August 2015.

Pre-assignment

Screening details:

533 were enrolled and screened. Subjects who met all eligibility criteria were randomized in a 2:1 ratio to receive once daily inhaled treatment with Pulmaquin or placebo.

Period 1

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

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | Active |

Arm description:

Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Linhaliq |
| Investigational medicinal product code | ARD-3150 |
| Other name | Pulmaquin |
| Pharmaceutical forms | Nebuliser solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

The administered dose was 189 mg (6 mL) of ciprofloxacin comprised of one vial of 135 mg (3mL) liposome-encapsulated ciprofloxacin dispersion and one vial of 54 mg (3mL) free ciprofloxacin solution given once daily by oral inhalation using a nebuliser; the dosing regimen was 6 cycles of 28 days on treatment, followed by 28 days off treatment.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Liquid mixture of empty liposomes and normal saline

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Nebuliser solution |
| Routes of administration | Inhalation use |

Dosage and administration details:

The administered dose was 6 mL placebo, comprised of one vial of 3 mL empty liposomes and one vial of 3 mL normal saline solution once daily by oral inhalation using a nebuliser; the dosing regimen was 6 cycles of 28 days on treatment, followed by 28 days off treatment.

| Number of subjects in period 1 | Active | Placebo |
|---------------------------------------|--------|---------|
| Started | 206 | 98 |
| Completed | 178 | 81 |
| Not completed | 28 | 17 |
| Adverse event, serious fatal | 1 | 2 |
| Physician decision | 3 | 1 |
| Consent withdrawn by subject | 13 | 11 |
| Adverse event, non-fatal | 4 | 2 |
| Other | 2 | - |
| Lost to follow-up | 3 | - |
| Lack of efficacy | 1 | - |
| Protocol deviation | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|--|---------|
| Reporting group title | Active |
| Reporting group description: Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin | |
| Reporting group title | Placebo |
| Reporting group description: Liquid mixture of empty liposomes and normal saline | |

| Reporting group values | Active | Placebo | Total |
|------------------------------------|--------|---------|-------|
| Number of subjects | 206 | 98 | 304 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|------------------|------------------|-----|
| Age continuous Units: years median full range (min-max) | 65.5 18 to 90 | 67.0 21 to 86 | - |
| Gender categorical Units: Subjects | | | |
| Female | 134 | 63 | 197 |
| Male | 72 | 35 | 107 |

End points

End points reporting groups

| | |
|--|---------|
| Reporting group title | Active |
| Reporting group description: | |
| Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Liquid mixture of empty liposomes and normal saline | |

Primary: Time to First Pulmonary Exacerbation

| | |
|---|--------------------------------------|
| End point title | Time to First Pulmonary Exacerbation |
| End point description: | |
| Median time to first pulmonary exacerbation | |
| End point type | Primary |
| End point timeframe: | |
| May 2014 to August 2016 | |

| End point values | Active | Placebo | | |
|----------------------------------|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 98 | | |
| Units: Number of days | | | | |
| median (confidence interval 95%) | 230.0 (187.0 to 341.0) | 158.0 (79.0 to 238.0) | | |

Statistical analyses

| | |
|---|-------------------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Active v Placebo |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0323 |
| Method | Stratified Unweighted Log-Rank Test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 0.97 |

Secondary: Frequency of Pulmonary Exacerbations

| | |
|-----------------|--------------------------------------|
| End point title | Frequency of Pulmonary Exacerbations |
|-----------------|--------------------------------------|

End point description:

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

End point timeframe:

May 2014 to August 2016

| End point values | Active | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 98 | | |
| Units: Number of Pulmonary Exacerbations | | | | |
| arithmetic mean (standard error) | 0.98 (± 0.09) | 1.47 (± 0.11) | | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Active v Placebo |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0006 |
| Method | Stratified Negative Binomial Regression |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 0.82 |

| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|------------------------|
| Comparison groups | Active v Placebo |

| | |
|---|-------------------|
| Number of subjects included in analysis | 304 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Counting Process |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.49 |
| upper limit | 0.76 |

Secondary: Frequency of Moderate and Severe Pulmonary Exacerbations

| | |
|-------------------------|--|
| End point title | Frequency of Moderate and Severe Pulmonary Exacerbations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| May 2014 to August 2016 | |

| End point values | Active | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 98 | | |
| Units: Number of Pulmonary Exacerbations | | | | |
| arithmetic mean (standard error) | 0.78 (± 0.10) | 1.27 (± 0.12) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Active v Placebo |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | Stratified Negative Binomial Regression |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 0.77 |

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Active v Placebo |
| Number of subjects included in analysis | 304 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Counting Process |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 0.71 |

Secondary: Frequency of Severe Pulmonary Exacerbations

| | |
|-------------------------|---|
| End point title | Frequency of Severe Pulmonary Exacerbations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| May 2014 to August 2016 | |

| | | | | |
|--|-----------------|-----------------|--|--|
| End point values | Active | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 206 | 98 | | |
| Units: Number of Pulmonary Exacerbations | | | | |
| arithmetic mean (standard error) | 0.14 (± 0.24) | 0.30 (± 0.25) | | |

Statistical analyses

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical Analysis 1 |
| Comparison groups | Active v Placebo |

| | |
|---|---|
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0031 |
| Method | Stratified Negative Binomial Regression |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.22 |
| upper limit | 0.74 |

| | |
|---|------------------------|
| Statistical analysis title | Statistical Analysis 2 |
| Comparison groups | Active v Placebo |
| Number of subjects included in analysis | 304 |
| Analysis specification | Post-hoc |
| Analysis type | superiority |
| P-value | = 0.001 |
| Method | Counting Process |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 0.71 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

May 2014 to August 2016

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Active |
|-----------------------|--------|

Reporting group description:

Liquid mixture of liposome-encapsulated and unencapsulated ciprofloxacin

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

Reporting group description:

Liquid mixture of empty liposomes and normal saline

| Serious adverse events | Active | Placebo | |
|---|-------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 35 / 206 (16.99%) | 28 / 98 (28.57%) | |
| number of deaths (all causes) | 2 | 4 | |
| number of deaths resulting from adverse events | 1 | 2 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| 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 | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Exercise tolerance decreased | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 2 / 98 (2.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| 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 | 3 / 206 (1.46%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial secretion retention | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cough | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 6 / 206 (2.91%) | 5 / 98 (5.10%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Increased viscosity of bronchial secretion | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 4 / 98 (4.08%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Rhonchi | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sputum increased | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 2 / 98 (2.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wheezing | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 3 / 206 (1.46%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Breath sounds abnormal | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (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 | | | |
| Avulsion fracture | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| 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 | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple injuries | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|----------------|--|
| Periorbital haematoma | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myoclonus | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (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 | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (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 | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| 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 | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tenosynovitis | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| 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 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 7 / 206 (3.40%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin graft infection | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sputum purulent | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 2 / 98 (2.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Active | Placebo | |
|---|--------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 179 / 206 (86.89%) | 95 / 98 (96.94%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 3 | 1 | |
| Keratoacanthoma | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 2 | |
| Myelofibrosis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vascular disorders | | | |
| Cryoglobulinaemia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hot flush | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 0 / 98 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Hypertension | | | |
| subjects affected / exposed | 9 / 206 (4.37%) | 3 / 98 (3.06%) | |
| occurrences (all) | 14 | 3 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Peripheral arterial occlusive disease | | | |

| | | | |
|--|-------------------|------------------|--|
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Application site irritation | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 1 / 98 (1.02%) | |
| occurrences (all) | 3 | 1 | |
| Chest discomfort | | | |
| subjects affected / exposed | 9 / 206 (4.37%) | 7 / 98 (7.14%) | |
| occurrences (all) | 10 | 9 | |
| Chest pain | | | |
| subjects affected / exposed | 11 / 206 (5.34%) | 4 / 98 (4.08%) | |
| occurrences (all) | 12 | 4 | |
| Chills | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 4 / 98 (4.08%) | |
| occurrences (all) | 5 | 7 | |
| Crepitations | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Device breakage | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Discomfort | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 1 | 1 | |
| Exercise tolerance decreased | | | |
| subjects affected / exposed | 54 / 206 (26.21%) | 32 / 98 (32.65%) | |
| occurrences (all) | 93 | 54 | |
| Fatigue | | | |

| | | |
|---|-------------------|------------------|
| subjects affected / exposed | 71 / 206 (34.47%) | 49 / 98 (50.00%) |
| occurrences (all) | 124 | 99 |
| Hernia pain | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Influenza like illness | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 0 / 98 (0.00%) |
| occurrences (all) | 3 | 0 |
| Malaise | | |
| subjects affected / exposed | 36 / 206 (17.48%) | 14 / 98 (14.29%) |
| occurrences (all) | 39 | 21 |
| Medical device site irritation | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Non-cardiac chest pain | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Oedema peripheral | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 6 / 98 (6.12%) |
| occurrences (all) | 1 | 7 |
| Pain | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 3 / 98 (3.06%) |
| occurrences (all) | 4 | 4 |
| Peripheral swelling | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Product taste abnormal | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 0 / 98 (0.00%) |
| occurrences (all) | 4 | 0 |
| Pyrexia | | |
| subjects affected / exposed | 42 / 206 (20.39%) | 24 / 98 (24.49%) |
| occurrences (all) | 62 | 33 |
| Systemic inflammatory response syndrome | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | | |
|--|----------------------|---------------------|--|
| Vaccination site discomfort subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Immune system disorders | | | |
| Allergy to animal subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Drug hypersensitivity subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Food allergy subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Seasonal allergy subjects affected / exposed occurrences (all) | 4 / 206 (1.94%) 4 | 0 / 98 (0.00%) 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia subjects affected / exposed occurrences (all) | 2 / 206 (0.97%) 2 | 0 / 98 (0.00%) 0 | |
| Prostatomegaly subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Asphyxia subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Asthma subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 2 / 98 (2.04%) 2 | |

| | | |
|---------------------------------------|--------------------|------------------|
| Asthmatic crisis | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Bronchospasm | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 2 |
| Catarrh | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Chronic obstructive pulmonary disease | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Cough | | |
| subjects affected / exposed | 137 / 206 (66.50%) | 71 / 98 (72.45%) |
| occurrences (all) | 285 | 192 |
| Diaphragmalgia | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dry throat | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 3 / 98 (3.06%) |
| occurrences (all) | 1 | 3 |
| Dysphonia | | |
| subjects affected / exposed | 6 / 206 (2.91%) | 1 / 98 (1.02%) |
| occurrences (all) | 6 | 1 |
| Dyspnoea | | |
| subjects affected / exposed | 106 / 206 (51.46%) | 53 / 98 (54.08%) |
| occurrences (all) | 234 | 144 |
| Dyspnoea exertional | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 2 / 98 (2.04%) |
| occurrences (all) | 2 | 2 |
| Epistaxis | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 0 / 98 (0.00%) |
| occurrences (all) | 5 | 0 |
| Haemoptysis | | |

| | | |
|--|-------------------|------------------|
| subjects affected / exposed | 25 / 206 (12.14%) | 18 / 98 (18.37%) |
| occurrences (all) | 36 | 30 |
| Hyperventilation | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Increased viscosity of bronchial secretion | | |
| subjects affected / exposed | 43 / 206 (20.87%) | 24 / 98 (24.49%) |
| occurrences (all) | 78 | 41 |
| Nasal congestion | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 3 / 98 (3.06%) |
| occurrences (all) | 5 | 3 |
| Oropharyngeal pain | | |
| subjects affected / exposed | 10 / 206 (4.85%) | 13 / 98 (13.27%) |
| occurrences (all) | 13 | 19 |
| Painful respiration | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Paranasal sinus discomfort | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pharyngeal erythema | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Pleurisy | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pleuritic pain | | |
| subjects affected / exposed | 6 / 206 (2.91%) | 1 / 98 (1.02%) |
| occurrences (all) | 7 | 1 |
| Pneumothorax | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Productive cough | | |
| subjects affected / exposed | 9 / 206 (4.37%) | 1 / 98 (1.02%) |
| occurrences (all) | 11 | 1 |

| | | |
|------------------------------|-------------------|------------------|
| Pulmonary embolism | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pulmonary hypertension | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Pulmonary pain | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rales | | |
| subjects affected / exposed | 13 / 206 (6.31%) | 5 / 98 (5.10%) |
| occurrences (all) | 20 | 9 |
| Respiratory failure | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Respiratory tract congestion | | |
| subjects affected / exposed | 9 / 206 (4.37%) | 8 / 98 (8.16%) |
| occurrences (all) | 11 | 8 |
| Rhinorrhoea | | |
| subjects affected / exposed | 11 / 206 (5.34%) | 9 / 98 (9.18%) |
| occurrences (all) | 12 | 13 |
| Rhonchi | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 3 / 98 (3.06%) |
| occurrences (all) | 4 | 6 |
| Sinus congestion | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 0 / 98 (0.00%) |
| occurrences (all) | 3 | 0 |
| Sleep apnoea syndrome | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Sputum discoloured | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 7 / 98 (7.14%) |
| occurrences (all) | 7 | 7 |
| Sputum increased | | |
| subjects affected / exposed | 99 / 206 (48.06%) | 62 / 98 (63.27%) |
| occurrences (all) | 186 | 155 |

| | | | |
|-----------------------------|-------------------|------------------|--|
| Sputum retention | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Tachypnoea | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 1 | |
| Throat irritation | | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 3 / 98 (3.06%) | |
| occurrences (all) | 4 | 6 | |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Wheezing | | | |
| subjects affected / exposed | 84 / 206 (40.78%) | 48 / 98 (48.98%) | |
| occurrences (all) | 149 | 114 | |
| Psychiatric disorders | | | |
| Abnormal dreams | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 2 / 98 (2.04%) | |
| occurrences (all) | 1 | 3 | |
| Anhedonia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Anxiety | | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 1 / 98 (1.02%) | |
| occurrences (all) | 4 | 1 | |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Depression | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 1 | |
| Emotional disorder | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Insomnia | | | |

| | | | |
|--------------------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 206 (0.00%) | 3 / 98 (3.06%) | |
| occurrences (all) | 0 | 3 | |
| Irritability | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Major depression | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Middle insomnia | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Mood altered | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mood swings | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 2 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) | |
| occurrences (all) | 0 | 3 | |
| Anticonvulsant drug level increased | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) | |
| occurrences (all) | 0 | 2 | |
| Aspergillus test positive | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| blood cortisol decreased | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Blood creatine increased | | | |

| | | |
|-------------------------------------|-------------------|------------------|
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Blood glucose increased | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Body temperature increased | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 1 / 98 (1.02%) |
| occurrences (all) | 3 | 1 |
| Breath sounds abnormal | | |
| subjects affected / exposed | 61 / 206 (29.61%) | 28 / 98 (28.57%) |
| occurrences (all) | 86 | 52 |
| C-reactive protein abnormal | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| C-reactive protein increased | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Chest X-ray abnormal | | |
| subjects affected / exposed | 7 / 206 (3.40%) | 2 / 98 (2.04%) |
| occurrences (all) | 8 | 2 |
| Crystal urine present | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Electrocardiogram change | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Forced expiratory volume decreased | | |
| subjects affected / exposed | 70 / 206 (33.98%) | 33 / 98 (33.67%) |
| occurrences (all) | 114 | 55 |
| Forced vital capacity decreased | | |
| subjects affected / exposed | 48 / 206 (23.30%) | 24 / 98 (24.49%) |
| occurrences (all) | 80 | 38 |
| Gamma-glutamyltransferase increased | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |

| | | |
|--|-----------------|----------------|
| Glomerular filtration rate decreased | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Heart rate increased | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hepatic enzyme increased | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| International normalised ratio fluctuation | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Liver function test abnormal | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lymph node palpable | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lymphocyte count increased | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 3 | 0 |
| Medication residue present | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Neutrophil count increased | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Platelet count increased | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Pseudomonas test positive | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pulmonary function test decreased | | |

| | | | |
|--|-------------------|------------------|--|
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 1 | 1 | |
| Spirometry abnormal | | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 1 / 98 (1.02%) | |
| occurrences (all) | 5 | 1 | |
| Sputum abnormal | | | |
| subjects affected / exposed | 24 / 206 (11.65%) | 15 / 98 (15.31%) | |
| occurrences (all) | 38 | 30 | |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 3 / 98 (3.06%) | |
| occurrences (all) | 2 | 3 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| White blood cell count increased | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| White blood cells urine positive | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| X-ray abnormal | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Animal scratch | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Arthropod bite | | | |

| | | |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Arthropod sting | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Avulsion fracture | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Back injury | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Contusion | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 0 / 98 (0.00%) |
| occurrences (all) | 8 | 0 |
| Fall | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 0 / 98 (0.00%) |
| occurrences (all) | 12 | 0 |
| Foot fracture | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 2 / 98 (2.04%) |
| occurrences (all) | 1 | 2 |
| Forearm fracture | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Head injury | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Hip fracture | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Joint dislocation | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Joint injury | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Laceration | | |

| | | | |
|------------------------------|-----------------|----------------|--|
| subjects affected / exposed | 5 / 206 (2.43%) | 2 / 98 (2.04%) | |
| occurrences (all) | 5 | 2 | |
| Ligament sprain | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 2 | |
| Limb injury | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 1 | |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 1 | 1 | |
| Post-traumatic neck syndrome | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Post-traumatic pain | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tooth fracture | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 1 | 1 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|-----------------------------|-----------------|----------------|--|
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 2 / 98 (2.04%) | |
| occurrences (all) | 3 | 2 | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Cor pulmonale chronic | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Palpitations | | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 2 / 98 (2.04%) | |
| occurrences (all) | 6 | 2 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nervous system disorders | | | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cluster headache | | | |

| | | |
|-----------------------------|-------------------|------------------|
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dementia | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| dizziness | | |
| subjects affected / exposed | 13 / 206 (6.31%) | 4 / 98 (4.08%) |
| occurrences (all) | 17 | 4 |
| Dizziness postural | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Dysgeusia | | |
| subjects affected / exposed | 13 / 206 (6.31%) | 7 / 98 (7.14%) |
| occurrences (all) | 36 | 7 |
| Essential tremor | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Headache | | |
| subjects affected / exposed | 23 / 206 (11.17%) | 14 / 98 (14.29%) |
| occurrences (all) | 33 | 24 |
| Hypogeusia | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lethargy | | |
| subjects affected / exposed | 49 / 206 (23.79%) | 20 / 98 (20.41%) |
| occurrences (all) | 87 | 46 |
| Migraine | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 2 / 98 (2.04%) |
| occurrences (all) | 1 | 2 |
| Neuralgia | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Neuropathy peripheral | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Paraesthesia | | |

| | | | |
|--------------------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) | |
| occurrences (all) | 0 | 2 | |
| Parkinson's disease | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Resting tremor | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 2 | |
| Sinus headache | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 0 / 98 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Somnolence | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 0 / 98 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Syncope | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 1 | |
| Tremor | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 2 / 98 (2.04%) | |
| occurrences (all) | 2 | 2 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 0 / 98 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Eosinophilia | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 3 / 98 (3.06%) | |
| occurrences (all) | 0 | 3 | |
| White blood cell disorder | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|------------------------------|-----------------|----------------|--|
| Ear and labyrinth disorders | | | |
| Ear discomfort | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear pain | | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 5 / 98 (5.10%) | |
| occurrences (all) | 6 | 5 | |
| Excessive cerumen production | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| External ear inflammation | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Neurosensory hypoacusis | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Tinnitus | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vertigo | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 2 / 98 (2.04%) | |
| occurrences (all) | 3 | 2 | |
| Vertigo positional | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 2 | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Dry eye | | | |

| | | | |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Eye haemorrhage | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye pain | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 1 | 1 | |
| Eye swelling | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Lacrimation increased | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Vitreous detachment | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitreous floaters | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 5 / 98 (5.10%) | |
| occurrences (all) | 7 | 5 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 5 / 98 (5.10%) | |
| occurrences (all) | 3 | 5 | |

| | | |
|-----------------------------|------------------|------------------|
| Abdominal tenderness | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Anorectal discomfort | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Anorectal varices | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Chronic gastritis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Constipation | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 2 / 98 (2.04%) |
| occurrences (all) | 5 | 2 |
| Dental caries | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Diarrhoea | | |
| subjects affected / exposed | 14 / 206 (6.80%) | 10 / 98 (10.20%) |
| occurrences (all) | 17 | 11 |
| Dry mouth | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 4 / 98 (4.08%) |
| occurrences (all) | 1 | 4 |
| Dyspepsia | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Dysphagia | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Epigastric discomfort | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Faecaloma | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |

| | | |
|----------------------------------|-----------------|----------------|
| Faeces soft | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Femoral hernia | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Flatulence | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Frequent bowel movements | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Gastritis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 3 / 98 (3.06%) |
| occurrences (all) | 1 | 3 |
| Gastrooesophageal reflux disease | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 1 / 98 (1.02%) |
| occurrences (all) | 5 | 1 |
| Gingival pain | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Haematochezia | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Haemorrhoids | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Haemorrhoids thrombosed | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Intestinal polyp | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Irritable bowel syndrome | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | |
|---------------------------------|------------------|----------------|
| Lip pain | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) |
| occurrences (all) | 0 | 2 |
| Lip swelling | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| mouth ulceration | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Nausea | | |
| subjects affected / exposed | 14 / 206 (6.80%) | 7 / 98 (7.14%) |
| occurrences (all) | 19 | 13 |
| Odynophagia | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Oesophagitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Portal hypertensive gastropathy | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Salivary gland enlargement | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Salivary hypersecretion | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Tongue ulceration | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Tooth impacted | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Toothache | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |

| | | | |
|---|----------------------|---------------------|--|
| Varices oesophageal subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Vomiting subjects affected / exposed occurrences (all) | 6 / 206 (2.91%) 6 | 4 / 98 (4.08%) 5 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis subjects affected / exposed occurrences (all) | 3 / 206 (1.46%) 3 | 0 / 98 (0.00%) 0 | |
| Gallbladder polyp subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Hepatic steatosis subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Actinic keratosis subjects affected / exposed occurrences (all) | 2 / 206 (0.97%) 2 | 0 / 98 (0.00%) 0 | |
| Alopecia subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Dermatitis subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Dry skin subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 1 / 98 (1.02%) 1 | |
| Eczema subjects affected / exposed occurrences (all) | 2 / 206 (0.97%) 2 | 1 / 98 (1.02%) 1 | |
| Erythema subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Hyperhidrosis | | | |

| | | |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Night sweats | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 1 / 98 (1.02%) |
| occurrences (all) | 3 | 1 |
| Onychomadesis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pain of skin | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Photosensitivity reaction | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Precancerous skin lesion | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Pruritus | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 4 / 98 (4.08%) |
| occurrences (all) | 3 | 4 |
| Purpura | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Rash | | |
| subjects affected / exposed | 7 / 206 (3.40%) | 3 / 98 (3.06%) |
| occurrences (all) | 7 | 5 |
| Rash generalised | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Rash maculo-papular | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rash pruritic | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Skin atrophy | | |

| | | | |
|---|----------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Skin disorder subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Skin lesion subjects affected / exposed occurrences (all) | 2 / 206 (0.97%) 2 | 2 / 98 (2.04%) 2 | |
| Skin reaction subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Renal and urinary disorders Bladder discomfort subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Haematuria subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 1 / 98 (1.02%) 1 | |
| Micturition disorder subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Nephrolithiasis subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 0 / 98 (0.00%) 0 | |
| Nocturia subjects affected / exposed occurrences (all) | 0 / 206 (0.00%) 0 | 1 / 98 (1.02%) 1 | |
| Pollakiuria subjects affected / exposed occurrences (all) | 1 / 206 (0.49%) 1 | 1 / 98 (1.02%) 1 | |
| Endocrine disorders Hypothyroidism | | | |

| | | | |
|---|------------------|----------------|--|
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 13 / 206 (6.31%) | 5 / 98 (5.10%) | |
| occurrences (all) | 14 | 5 | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Back pain | | | |
| subjects affected / exposed | 8 / 206 (3.88%) | 3 / 98 (3.06%) | |
| occurrences (all) | 8 | 4 | |
| Exostosis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fibromyalgia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Joint effusion | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Joint swelling | | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 1 / 98 (1.02%) | |
| occurrences (all) | 5 | 2 | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 1 | 1 | |
| Muscle twitching | | | |

| | | |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Musculoskeletal chest pain | | |
| subjects affected / exposed | 8 / 206 (3.88%) | 1 / 98 (1.02%) |
| occurrences (all) | 8 | 1 |
| Musculoskeletal discomfort | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Musculoskeletal pain | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 0 / 98 (0.00%) |
| occurrences (all) | 5 | 0 |
| Musculoskeletal stiffness | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Myalgia | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 7 / 98 (7.14%) |
| occurrences (all) | 10 | 8 |
| Neck pain | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 4 / 98 (4.08%) |
| occurrences (all) | 1 | 4 |
| Osteoarthritis | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 1 / 98 (1.02%) |
| occurrences (all) | 5 | 1 |
| Osteoporosis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 2 / 98 (2.04%) |
| occurrences (all) | 1 | 2 |
| pain in extremity | | |
| subjects affected / exposed | 8 / 206 (3.88%) | 2 / 98 (2.04%) |
| occurrences (all) | 8 | 2 |
| Pain in jaw | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) |
| occurrences (all) | 0 | 2 |
| Plantar fasciitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rheumatoid arthritis | | |

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|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 1 | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Spinal osteoarthritis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 1 | 1 | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Tendon calcification | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Tendon disorder | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tendonitis | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tenosynovitis stenosans | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |
| Abdominal hernia infection | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 0 / 98 (0.00%) | |
| occurrences (all) | 4 | 0 | |

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|-------------------------------------|-----------------|----------------|
| Bronchitis viral | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Bronchopulmonary aspergillosis | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Candida infection | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Catheter site infection | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cellulitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Chlamydial infection | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Chronic sinusitis | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 3 | 1 |
| Conjunctivitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Cystitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Diverticulitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Ear infection | | |
| subjects affected / exposed | 4 / 206 (1.94%) | 3 / 98 (3.06%) |
| occurrences (all) | 5 | 3 |
| Escherichia urinary tract infection | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |

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|-----------------------------------|-----------------|----------------|
| Fungal infection | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 0 / 98 (0.00%) |
| occurrences (all) | 3 | 0 |
| Fungal skin infection | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Gastroenteritis | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Gastroenteritis viral | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Helicobacter infection | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Herpes zoster | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Infectious disease carrier | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Influenza | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 3 / 98 (3.06%) |
| occurrences (all) | 2 | 4 |
| Labyrinthitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Laryngitis | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Localised infection | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lower respiratory tract infection | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |

| | | |
|---|------------------|----------------|
| Lower respiratory tract infection bacterial | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Lyme disease | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Nasopharyngitis | | |
| subjects affected / exposed | 13 / 206 (6.31%) | 6 / 98 (6.12%) |
| occurrences (all) | 15 | 7 |
| Nocardiosis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Oesophageal candidiasis | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Oral candidiasis | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 4 / 98 (4.08%) |
| occurrences (all) | 3 | 6 |
| Oral herpes | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) |
| occurrences (all) | 0 | 1 |
| Otitis externa | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) |
| occurrences (all) | 0 | 2 |
| Otitis media | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Otitis media acute | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) |
| occurrences (all) | 1 | 1 |
| Pharyngitis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Pneumonia | | |

| | | |
|-----------------------------------|-------------------|------------------|
| subjects affected / exposed | 3 / 206 (1.46%) | 0 / 98 (0.00%) |
| occurrences (all) | 3 | 0 |
| Pneumonia bacterial | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Respiratory tract infection | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Respiratory tract infection viral | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rhinitis | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 4 / 98 (4.08%) |
| occurrences (all) | 5 | 7 |
| Sepsis | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 1 | 0 |
| Sinusitis | | |
| subjects affected / exposed | 13 / 206 (6.31%) | 4 / 98 (4.08%) |
| occurrences (all) | 16 | 6 |
| Skin candida | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) |
| occurrences (all) | 2 | 0 |
| Sputum purulent | | |
| subjects affected / exposed | 52 / 206 (25.24%) | 35 / 98 (35.71%) |
| occurrences (all) | 90 | 59 |
| Staphylococcal infection | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) |
| occurrences (all) | 2 | 1 |
| Tonsillitis | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) |
| occurrences (all) | 0 | 2 |
| Tooth abscess | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 2 / 98 (2.04%) |
| occurrences (all) | 1 | 2 |
| Tooth infection | | |

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|---|------------------|----------------|--|
| subjects affected / exposed | 3 / 206 (1.46%) | 1 / 98 (1.02%) | |
| occurrences (all) | 4 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 8 / 206 (3.88%) | 1 / 98 (1.02%) | |
| occurrences (all) | 8 | 1 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 10 / 206 (4.85%) | 3 / 98 (3.06%) | |
| occurrences (all) | 13 | 5 | |
| Viral infection | | | |
| subjects affected / exposed | 3 / 206 (1.46%) | 2 / 98 (2.04%) | |
| occurrences (all) | 3 | 2 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 2 / 98 (2.04%) | |
| occurrences (all) | 0 | 2 | |
| Vulvovaginal candidiasis | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 4 / 98 (4.08%) | |
| occurrences (all) | 2 | 5 | |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 2 | |
| Metabolism and nutrition disorders | | | |
| Abnormal loss of weight | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 5 / 206 (2.43%) | 0 / 98 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Fluid retention | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |

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| Gout | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 1 | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 2 / 206 (0.97%) | 1 / 98 (1.02%) | |
| occurrences (all) | 2 | 1 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypophagia | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 1 / 206 (0.49%) | 0 / 98 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 206 (0.00%) | 1 / 98 (1.02%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported