# Clinical trial results:
# A Dose-Ranging Study of the Efficacy and Safety of Bardoxolone Methyl in Patients with Pulmonary Hypertension (PH) - LARIAT

## Summary

| | |
|---|---|
| EudraCT number | 2016-004793-17 |
| Trial protocol | DE GB ES |
| Global end of trial date | 16 May 2018 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 01 December 2021 |
| First version publication date | 01 December 2021 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 402-C-1302 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02036970 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Reata Pharmaceuticals, Inc. |
| Sponsor organisation address | 5320 Legacy Drive, Plano, United States, 75024 |
| Public contact | Kris Loerwald, Reata Pharmaceuticals, Inc., 972 865-2219, MedicalAffairs-Team@reatapharma.com |
| Scientific contact | Kris Loerwald, Reata Pharmaceuticals, Inc., 972 865-2219, MedicalAffairs-Team@reatapharma.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 | 17 December 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 19 January 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 May 2018 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This study assesses the safety and efficacy of bardoxolone methyl relative to placebo in patients with pulmonary hypertension to determine the recommended dose range, evaluate the change from baseline in 6-minute walk distance (6MWD) and determine the effect of Bardoxolone methyl in pulmonary hypertension associated with connective tissue disease, interstitial lung disease, and idiopathic etiologies, including subsets of patients with WHO Group III or WHO Group V PH following 16 weeks of study participation.

Protection of trial subjects:

A Protocol Safety Review Committee (PSRC) assessed the starting dose and each new dose level of bardoxolone methyl for safety and tolerability based on review of all available data for this study at the time of each review. PSRC reviews occurred after the Week 4 data are available for the first eight patients enrolled at each new dose level combined across Cohorts 1 and 2 (i.e., the 6MWD ≤ 450 m and 6MWD > 450 m cohorts). Upon completion of the dose ranging portion of the study, the PSRC continued to meet at regular intervals (approximately quarterly) to monitor safety of all patients, including those enrolled in Cohorts 3 and 4. The PSRC included at a minimum a Sponsor representative, a cardiologist, and a statistician. PSRC also assessed for general safety and specific signs and symptoms of fluid overload. The PSRC assessment included a dose level recommendation based on clinical evaluation of protocol specified assessments for subsequent cohorts to escalate to a higher dose, proceed to a lower dose, or maintain the current dose. The PSRC also could recommend stopping dosing in current cohorts.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 01 June 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 | United States: 164 |
| Country: Number of subjects enrolled | Germany: 2 |
| Worldwide total number of subjects | 166 |
| EEA total number of subjects | 2 |

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) | 124 |
| From 65 to 84 years | 42 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16). Part 2: Open-label extension period (Week 16 onwards). Part 2 is the extension period and patients were to stay until study drug became available through extended access program [Study 402-C-1602]. Each participant in Part 2 was also in Part 1.

### Period 1

| | |
|---|---|
| Period 1 title | Part 1: Day 1 Through Week 16 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Subject |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Part 1:Dose Ranging Bardoxolone Methyl 2.5mg |

Arm description:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 2.5mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 1:Dose-Ranging Bardoxolone Methyl 5mg |

Arm description:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 5mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 1:Dose-Ranging Bardoxolone Methyl 10mg |

Arm description:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2

(Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 10mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 1:Dose-Ranging Bardoxolone Methyl 20mg |

Arm description:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 20mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 1:Dose-Ranging Placebo 2.5mg |

Arm description:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo Capsules |
| Investigational medicinal product code | Placebo |
| Other name | Placebo |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 1: Dose-Ranging Placebo 5 mg |

Arm description:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo Capsules 5mg |
| Investigational medicinal product code | Placebo |
| Other name | Placebo |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2

| **Arm title** | Part 1: Dose-Ranging Placebo 10 mg |
|---|---|

Arm description:

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo Capsules 10mg |
| Investigational medicinal product code | Placebo |
| Other name | Placebo |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

| **Arm title** | Part 1: Dose-Ranging Placebo 20 mg |
|---|---|

Arm description:

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo Capsules 20mg |
| Investigational medicinal product code | Placebo |
| Other name | Placebo |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| **Arm title** | Part 1: Dose Titration: Bardoxolone Methyl 10 mg |
|---|---|

Arm description:

Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 10mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)

| **Arm title** | Part 1: Dose Titration: Placebo 10 mg |
|---|---|

Arm description:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo Capsules 10mg |
| Investigational medicinal product code | Placebo |
| Other name | Placebo |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

| **Number of subjects in period 1** | Part 1:Dose Ranging Bardoxolone Methyl 2.5mg | Part 1:Dose-Ranging Bardoxolone Methyl 5mg | Part 1:Dose-Ranging Bardoxolone Methyl 10mg |
|---|---|---|---|
| Started | 6 | 12 | 11 |
| Completed | 5 | 12 | 7 |
| Not completed | 1 | 0 | 4 |
| Consent withdrawn by subject | - | - | - |
| Adverse event, non-fatal | - | - | 3 |
| Death | - | - | - |
| Progressive Disease | - | - | - |
| Protocol deviation | 1 | - | 1 |

| **Number of subjects in period 1** | Part 1:Dose-Ranging Bardoxolone Methyl 20mg | Part 1:Dose-Ranging Placebo 2.5mg | Part 1: Dose-Ranging Placebo 5 mg |
|---|---|---|---|
| Started | 12 | 2 | 4 |
| Completed | 9 | 1 | 3 |
| Not completed | 3 | 1 | 1 |
| Consent withdrawn by subject | - | 1 | - |
| Adverse event, non-fatal | 2 | - | 1 |
| Death | - | - | - |
| Progressive Disease | 1 | - | - |
| Protocol deviation | - | - | - |

| **Number of subjects in period 1** | Part 1: Dose-Ranging Placebo 10 mg | Part 1: Dose-Ranging Placebo 20 mg | Part 1: Dose Titration: Bardoxolone Methyl 10 mg |
|---|---|---|---|
| Started | 3 | 4 | 74 |
| Completed | 3 | 3 | 66 |
| Not completed | 0 | 1 | 8 |
| Consent withdrawn by subject | - | - | 2 |
| Adverse event, non-fatal | - | 1 | 3 |

| | | | |
|---|---|---|---|
| Death | - | - | 1 |
| Progressive Disease | - | - | - |
| Protocol deviation | - | - | 2 |

| **Number of subjects in period 1** | Part 1: Dose Titration: Placebo 10 mg |
|---|---|
| Started | 38 |
| Completed | 33 |
| Not completed | 5 |
| Consent withdrawn by subject | 4 |
| Adverse event, non-fatal | 1 |
| Death | - |
| Progressive Disease | - |
| Protocol deviation | - |

## Period 2

| | |
|---|---|
| Period 2 title | Part 2 Open-label extension: Week 16 On |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Part 2: Open-Label Bardoxolone Methyl 2.5 mg |

Arm description:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 2.5mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 2: Open-Label Bardoxolone Methyl 5 mg |

Arm description:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

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

| | |
|---|---|
| Investigational medicinal product name | Bardoxolone methyl capsules 5mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 2: Open-Label Bardoxolone Methyl 10 mg |

Arm description:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 10mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards

| | |
|---|---|
| **Arm title** | Part 2: Open-Label Bardoxolone Methyl 20 mg |

Arm description:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 20 mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 2: Bardoxolone Methyl 2.5 mg |

Arm description:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 2.5mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 2: Bardoxolone Methyl 5 mg |

Arm description:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 5mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 2: Bardoxolone Methyl 10 mg |

Arm description:

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 10mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 2: Bardoxolone Methyl 20 mg |

Arm description:

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone methyl capsules 20mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| | |
|---|---|
| **Arm title** | Part 2: Bardoxolone Methyl 10 mg |

Arm description:

Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)

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

| | |
|---|---|
| Investigational medicinal product name | Bardoxolone methyl capsules 10mg |
| Investigational medicinal product code | RTA 402 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Bardoxolone methyl capsules 10mg taken orally once daily in Part 2 Open label.

| | |
|---|---|
| Investigational medicinal product name | Bardoxolone methyl capsules 10mg |
| Investigational medicinal product code | RTA 402 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Bardoxolone methyl capsules 10mg taken orally once daily in Part 2 (Open label)

| | |
|---|---|
| **Arm title** | Part 2: Bardoxolone methyl capsules 10mg |

Arm description:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Bardoxolone Methyl 10 mg |
| Investigational medicinal product code | RTA 402 |
| Other name | RTA 402 capsules |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

| **Number of subjects in period 2[1]** | Part 2: Open-Label Bardoxolone Methyl 2.5 mg | Part 2: Open-Label Bardoxolone Methyl 5 mg | Part 2: Open-Label Bardoxolone Methyl 10 mg |
|---|---|---|---|
| Started | 5 | 11 | 6 |
| Completed | 5 | 6 | 3 |
| Not completed | 0 | 5 | 3 |
| Consent withdrawn by subject | - | 1 | 1 |
| Adverse event, non-fatal | - | 2 | 1 |
| Progressive Disease | - | 2 | 1 |
| Protocol deviation | - | - | - |

| **Number of subjects in period 2[1]** | Part 2: Open-Label Bardoxolone Methyl 20 mg | Part 2: Bardoxolone Methyl 2.5 mg | Part 2: Bardoxolone Methyl 5 mg |
|---|---|---|---|
| Started | 9 | 1 | 3 |
| Completed | 7 | 0 | 3 |
| Not completed | 2 | 1 | 0 |
| Consent withdrawn by subject | - | - | - |
| Adverse event, non-fatal | 1 | 1 | - |

| | | | |
|---|---|---|---|
| Progressive Disease | 1 | - | - |
| Protocol deviation | - | - | - |

| **Number of subjects in period 2[1]** | Part 2: Bardoxolone Methyl 10 mg | Part 2: Bardoxolone Methyl 20 mg | Part 2: Bardoxolone Methyl 10 mg |
|---|---|---|---|
| Started | 3 | 3 | 63 |
| Completed | 2 | 2 | 54 |
| Not completed | 1 | 1 | 9 |
| Consent withdrawn by subject | - | - | 3 |
| Adverse event, non-fatal | 1 | - | 6 |
| Progressive Disease | - | - | - |
| Protocol deviation | - | 1 | - |

| **Number of subjects in period 2[1]** | Part 2: Bardoxolone methyl capsules 10mg |
|---|---|
| Started | 33 |
| Completed | 28 |
| Not completed | 5 |
| Consent withdrawn by subject | - |
| Adverse event, non-fatal | 3 |
| Progressive Disease | 2 |
| Protocol deviation | - |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 4 Patients total that completed Part 1 of the trial, elected not to continue into Part 2 of the trial therefore, the number of subjects starting the period will not be consistent with the number completing the preceding period.

## Baseline characteristics

### Reporting groups

| Reporting group title | Part 1:Dose Ranging Bardoxolone Methyl 2.5mg |
|---|---|
| Reporting group description: | |
| Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Bardoxolone Methyl 5mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Bardoxolone Methyl 10mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Bardoxolone Methyl 20mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Placebo 2.5mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose-Ranging Placebo 5 mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose-Ranging Placebo 10 mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose-Ranging Placebo 20 mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose Titration: Bardoxolone Methyl 10 mg |
| Reporting group description: | |
| Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose Titration: Placebo 10 mg |
| Reporting group description: | |
| Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards | |

| Reporting group values | Part 1:Dose Ranging Bardoxolone Methyl 2.5mg | Part 1:Dose-Ranging Bardoxolone Methyl 5mg | Part 1:Dose-Ranging Bardoxolone Methyl 10mg |
|---|---|---|---|
| Number of subjects | 6 | 12 | 11 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years | | | |
| arithmetic mean | 52.5 | 52.8 | 50.6 |
| standard deviation | ± 7.15 | ± 14.84 | ± 16.33 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 10 | 8 |
| Male | 2 | 2 | 3 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 2 | 3 | 0 |
| Not Hispanic or Latino | 4 | 9 | 11 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asia | 0 | 0 | 0 |
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 1 | 1 |
| White | 6 | 11 | 9 |
| More than one Race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 1 |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters | | | |
| arithmetic mean | 412 | 425.8 | 385.7 |
| standard deviation | ± 19.7 | ± 81 | ± 55.45 |

| Reporting group values | Part 1:Dose-Ranging Bardoxolone Methyl 20mg | Part 1:Dose-Ranging Placebo 2.5mg | Part 1: Dose-Ranging Placebo 5 mg |
|---|---|---|---|
| Number of subjects | 12 | 2 | 4 |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years | | | |
| arithmetic mean | 49.6 | 53 | 39.5 |
| standard deviation | ± 13.06 | ± 15.56 | ± 11.27 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 11 | 1 | 4 |
| Male | 1 | 1 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 1 |
| Not Hispanic or Latino | 11 | 2 | 3 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asia | 0 | 0 | 0 |
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 3 |
| White | 12 | 2 | 1 |
| More than one Race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters | | | |
| arithmetic mean | 454.5 | 358 | 418.9 |
| standard deviation | ± 93.01 | ± 96.17 | ± 71.18 |

| **Reporting group values** | Part 1: Dose-Ranging Placebo 10 mg | Part 1: Dose-Ranging Placebo 20 mg | Part 1: Dose Titration: Bardoxolone Methyl 10 mg |
|---|---|---|---|
| Number of subjects | 3 | 4 | 74 |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years | | | |
| arithmetic mean | 54.7 | 51.3 | 56.4 |
| standard deviation | ± .58 | ± 8.54 | ± 12.41 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 2 | 3 | 54 |
| Male | 1 | 1 | 20 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 12 |
| Not Hispanic or Latino | 3 | 4 | 62 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asia | 0 | 0 | 2 |
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 17 |
| White | 3 | 4 | 54 |
| More than one Race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 1 |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters | | | |
| arithmetic mean | 367 | 449.3 | 380.8 |
| standard deviation | ± 46.02 | ± 84.64 | ± 96.46 |

| **Reporting group values** | Part 1: Dose Titration: Placebo 10 mg | Total | |
|---|---|---|---|
| Number of subjects | 38 | 166 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | | 0 | |

| | | | |
|---|---|---|---|
| Preterm newborn infants (gestational age < 37 wks) | | 0 | |
| Newborns (0-27 days) | | 0 | |
| Infants and toddlers (28 days-23 months) | | 0 | |
| Children (2-11 years) | | 0 | |
| Adolescents (12-17 years) | | 0 | |
| Adults (18-64 years) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years | | | |
| arithmetic mean | 55.6 | | |
| standard deviation | ± 12.7 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 27 | 124 | |
| Male | 11 | 42 | |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 7 | 26 | |
| Not Hispanic or Latino | 31 | 140 | |
| Unknown or Not Reported | 0 | 0 | |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | |
| Asia | 0 | 2 | |
| Native Hawaiian or Pacific Islander | 1 | 1 | |
| Black or African American | 9 | 31 | |
| White | 28 | 130 | |
| More than one Race | 0 | 0 | |
| Unknown or Not Reported | 0 | 2 | |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters | | | |
| arithmetic mean | 395.2 | | |
| standard deviation | ± 84.99 | - | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 2.5 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 2.5 mg once-daily from Week 16 onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 5mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 5 mg once-daily from Week 16 onwards.

| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 10 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 wer eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 10 mg once-daily from Week 16 onwards.

| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 20 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 20 mg once-daily from Week 16 onwards.

| Subject analysis set title | Part 2: Bardoxolone Methyl 2.5 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 2.5 mg once-daily from Week 16 and onwards.

| Subject analysis set title | Part 2: Bardoxolone Methyl 5 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 5 mg once-daily from Week 16 and onwards.

| Subject analysis set title | Part 2: Bardoxolone Methyl 10 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.

| Subject analysis set title | Part 2: Bardoxolone Methyl 20 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 20 mg once-daily from Week 16 and onwards.

| Subject analysis set title | Part 2: Bardoxolone Methyl 10 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received the same bardoxolone methyl dose once-daily from Week 16 and onwards.

| Subject analysis set title | Part 2: Bardoxolone Methyl 10 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from Week 20 and onwards.

| Subject analysis set title | Part 2: Total |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Open-label extension period (Week 16 and onwards)

| Subject analysis set title | Change from Baseline though Week 16 for participants with PH |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 1: Dose Titration: Bardoxolone Methyl 10 mg

Participants were randomized to receive bardoxolone methyl 10 mg capsules. Participants initially started with bardoxolone methyl 5 mg once-daily from Day 1 and titrated to bardoxolone methyl 10 mg once-daily starting at Week 4 up to Week 16.

| | |
|---|---|
| Subject analysis set title | Change from Baseline though Week 16 for participants with PH |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description:<br>Part 1: Dose Titration: Placebo 10 mg | |

| **Reporting group values** | Part 2: Open-Label Bardoxolone Methyl 2.5 mg | Part 2: Open-Label Bardoxolone Methyl 5mg | Part 2: Open-Label Bardoxolone Methyl 10 mg |
|---|---|---|---|
| Number of subjects | 5 | 11 | 6 |
| Age categorical<br>Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years | | | |
| arithmetic mean | 54.6 | 53.4 | 59.2 |
| standard deviation | ± 5.55 | ± 14.4 | ± 10.26 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 4 | 9 | 4 |
| Male | 1 | 2 | 2 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 2 | 2 | 0 |
| Not Hispanic or Latino | 3 | 9 | 6 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asia | 0 | 0 | 0 |
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 1 | 0 |
| White | 5 | 10 | 5 |
| More than one Race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 1 |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters | | | |
| arithmetic mean | | | |

| | | | |
|---|---|---|---|
| standard deviation | ± | ± | ± |

| **Reporting group values** | Part 2: Open-Label Bardoxolone Methyl 20 mg | Part 2: Bardoxolone Methyl 2.5 mg | Part 2: Bardoxolone Methyl 5 mg |
|---|---|---|---|
| Number of subjects | 9 | 1 | 3 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years<br>arithmetic mean<br>standard deviation | <br>51<br>± 14.76 | <br>64<br>± 0 | <br>40<br>± 13.75 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 9 | 1 | 3 |
| Male | 0 | 0 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 9 | 1 | 3 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asia | 0 | 0 | 0 |
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 3 |
| White | 9 | 1 | 0 |
| More than one Race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters<br>arithmetic mean<br>standard deviation | <br><br>± | <br><br>± | <br><br>± |

| Reporting group values | Part 2: Bardoxolone Methyl 10 mg | Part 2: Bardoxolone Methyl 20 mg | Part 2: Bardoxolone Methyl 10 mg |
|---|---|---|---|
| Number of subjects | 3 | 3 | 63 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years | | | |
| arithmetic mean | 54.7 | 47.7 | 56.5 |
| standard deviation | ± .58 | ± 5.69 | ± 12.23 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2 | 3 | 47 |
| Male | 1 | 0 | 16 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 10 |
| Not Hispanic or Latino | 3 | 3 | 53 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaskan Native | 0 | 0 | 0 |
| Asia | 0 | 0 | 1 |
| Native Hawaiian or Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 14 |
| White | 3 | 3 | 47 |
| More than one Race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 1 |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |

| Reporting group values | Part 2: Bardoxolone Methyl 10 mg | Part 2: Total | Change from Baseline though Week 16 for participants with PH |
|---|---|---|---|

| Number of subjects | 33 | 137 | 70 |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years<br>arithmetic mean<br>standard deviation | <br>56.7<br>± 12.44 | <br>55.5<br>± 12.38 | <br><br>± |
| Gender categorical<br>Units: Subjects | | | |
| Female<br>Male | 24<br>9 | 106<br>31 | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported | 7<br>26<br>0 | 21<br>116<br>0 | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native<br>Asia<br>Native Hawaiian or Pacific Islander<br>Black or African American<br>White<br>More than one Race<br>Unknown or Not Reported | 0<br>0<br>0<br>5<br>28<br>0<br>0 | 0<br>1<br>0<br>23<br>111<br>0<br>2 | |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters<br>arithmetic mean<br>standard deviation | <br><br>± | <br><br>± | <br><br>± |

| **Reporting group values** | Change from Baseline though Week 16 for participants with PH | | |
|---|---|---|---|
| Number of subjects | 70 | | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous | | | |
| Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16)<br>Part 2: Open-label extension period (Week 16 and onwards | | | |
| Units: years<br>arithmetic mean<br>standard deviation | ± | | |
| Gender categorical<br>Units: Subjects | | | |
| Female<br>Male | | | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported | | | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaskan Native<br>Asia<br>Native Hawaiian or Pacific Islander<br>Black or African American<br>White<br>More than one Race<br>Unknown or Not Reported | | | |
| 6-Minute Walk Test (6MWT)[1] | | | |
| [1] Measure Analysis Population Description: Modified Intent-to-treat (mITT) population, which included all randomized patients who received at least 28 doses of study treatment, did not undergo heart or lung transplantation during the treatment period, and performed at least one-post baseline 6MWT assessment. Only Part 1 patients are included since the primary outcome is the change from baseline in 6MWD through Week 16 | | | |
| Units: Meters<br>arithmetic mean<br>standard deviation | ± | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Part 1:Dose Ranging Bardoxolone Methyl 2.5mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Bardoxolone Methyl 5mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Bardoxolone Methyl 10mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Bardoxolone Methyl 20mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1:Dose-Ranging Placebo 2.5mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose-Ranging Placebo 5 mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose-Ranging Placebo 10 mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose-Ranging Placebo 20 mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose Titration: Bardoxolone Methyl 10 mg |
| Reporting group description: | |
| Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards) | |
| Reporting group title | Part 1: Dose Titration: Placebo 10 mg |
| Reporting group description: | |
| Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards | |
| Reporting group title | Part 2: Open-Label Bardoxolone Methyl 2.5 mg |
| Reporting group description: | |
| Participants received bardoxolone methyl 2.5 mg once-daily in Part 1 (Day 1 to Week 16). Participants | |

who continued to Part 2 continued to receive the same bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Open-Label Bardoxolone Methyl 5 mg |
|---|---|

Reporting group description:

Participants received bardoxolone methyl 5 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Open-Label Bardoxolone Methyl 10 mg |
|---|---|

Reporting group description:

Participants received bardoxolone methyl 10 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards

| Reporting group title | Part 2: Open-Label Bardoxolone Methyl 20 mg |
|---|---|

Reporting group description:

Participants received bardoxolone methyl 20 mg once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 continued to receive the same bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Bardoxolone Methyl 2.5 mg |
|---|---|

Reporting group description:

Participants received bardoxolone methyl 2.5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 2.5 mg once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Bardoxolone Methyl 5 mg |
|---|---|

Reporting group description:

Participants received bardoxolone methyl 5 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 5 mg once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Bardoxolone Methyl 10 mg |
|---|---|

Reporting group description:

Participants received bardoxolone methyl 10 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 10 mg once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Bardoxolone Methyl 20 mg |
|---|---|

Reporting group description:

Participants received bardoxolone methyl 20 mg matching placebo capsules once-daily in Part 1 (Day 1 to Week 16). Participants who continued to Part 2 received bardoxolone methyl 20 mg once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Bardoxolone Methyl 10 mg |
|---|---|

Reporting group description:

Participants in Part 1 started with bardoxolone methyl 5 mg once-daily from Day 1 and escalated to bardoxolone methyl 10 mg once-daily starting at Week 4 thru Week 16. Participants who continued to Part 2 continued to receive the same bardoxolone methyl dose once-daily in Part 2 (Week 16 and onwards)

| Reporting group title | Part 2: Bardoxolone methyl capsules 10mg |
|---|---|

Reporting group description:

Participants in Part 1 received Placebo once-daily from Day 1 thru Week 16. Participants who continued to Part 2 initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from week 20 onwards

| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 2.5 mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 2.5 mg once-daily from Week 16 onwards.

| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 5mg |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 5 mg once-daily from Week 16 onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 10 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 wer eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 10 mg once-daily from Week 16 onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Open-Label Bardoxolone Methyl 20 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 20 mg once-daily from Week 16 onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Bardoxolone Methyl 2.5 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 2.5 mg once-daily from Week 16 and onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Bardoxolone Methyl 5 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 5 mg once-daily from Week 16 and onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Bardoxolone Methyl 10 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Bardoxolone Methyl 20 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 20 mg once-daily from Week 16 and onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Bardoxolone Methyl 10 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and received the same bardoxolone methyl dose once-daily from Week 16 and onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Bardoxolone Methyl 10 mg |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Participants who completed treatment in Part 1 were eligible to continue to the extension Part 2 and initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from Week 20 and onwards.

| | |
|---|---|
| Subject analysis set title | Part 2: Total |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 2: Open-label extension period (Week 16 and onwards)

| | |
|---|---|
| Subject analysis set title | Change from Baseline though Week 16 for participants with PH |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 1:  Dose Titration: Bardoxolone Methyl 10 mg

Participants were randomized to receive bardoxolone methyl 10 mg capsules. Participants initially started with bardoxolone methyl 5 mg once-daily from Day 1 and titrated to bardoxolone methyl 10 mg once-daily starting at Week 4 up to Week 16.

| | |
|---|---|
| Subject analysis set title | Change from Baseline though Week 16 for participants with PH |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

Part 1: Dose Titration: Placebo 10 mg

## Primary: Change From Baseline Though Week 16 in 6-Minute Walk Distance (6MWD) for Bardoxolone Methyl Compared to Placebo

| End point title | Change From Baseline Though Week 16 in 6-Minute Walk Distance (6MWD) for Bardoxolone Methyl Compared to Placebo |
|---|---|

End point description:

Overall treatment effect in exercise capacity, as measured by the total distance walked in 6 minutes (6MWD) mean change from baseline though Week 16. A lower 6MWD reflects greater severity thus, a positive change from baseline suggests an improvement.

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

End point timeframe:

Baseline through Week 16

| **End point values** | Part 1:Dose Ranging Bardoxolone Methyl 2.5mg | Part 1:Dose-Ranging Bardoxolone Methyl 5mg | Part 1:Dose-Ranging Bardoxolone Methyl 10mg | Part 1:Dose-Ranging Bardoxolone Methyl 20mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 | 12 | 9 | 10 |
| Units: Meters | | | | |
| arithmetic mean (standard deviation) | 32.5 (± 29.14) | 24 (± 30.08) | 3.4 (± 31.28) | -3.2 (± 39.53) |

| **End point values** | Part 1:Dose-Ranging Placebo 2.5mg | Part 1: Dose-Ranging Placebo 5 mg | Part 1: Dose-Ranging Placebo 10 mg | Part 1: Dose-Ranging Placebo 20 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 4 | 3 | 4 |
| Units: Meters | | | | |
| arithmetic mean (standard deviation) | 20.3 (± 13.08) | 24.6 (± 59.4) | 23.8 (± 34.54) | -21.8 (± 4.17) |

| **End point values** | Part 1: Dose Titration: Bardoxolone Methyl 10 mg | Part 1: Dose Titration: Placebo 10 mg | Change from Baseline though Week 16 for participants with PH | Change from Baseline though Week 16 for participants with PH |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 29 | 17 | 41[1] | 21[2] |
| Units: Meters | | | | |
| arithmetic mean (standard deviation) | 13.9 (± 41.15) | 19.4 (± 21.06) | 7.6 (± 32.01) | 10.8 (± 32.01) |

Notes:

[1] - Change from Baseline though Week 16 for participants with PH in the Part 1: Dose Titration Bard 10mg

[2] - Change from Baseline though Week 16 for participants w/PH in the Part 1 Dose Titration Placebo 10mg

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

Comparison Group Selection Part 1: Dose-Ranging Bardoxolone Methyl 2.5 mg/Part 2: Open-Label, Part 1: Dose-Ranging Bardoxolone Methyl 5 mg/Part 2: Open-Label, Part 1: Dose-Ranging Bardoxolone Methyl 10 mg/Part 2: Open-Label, Part 1: Dose-Ranging Bardoxolone Methyl 20 mg/Part 2: Open-Label, Part 1: Dose-Ranging Placebo 2.5 mg/Part 2: Bardoxolone Methyl 2.5 mg, Part 1: Dose-Ranging Placebo 5 mg/Part 2: Bardoxolone Methyl 5 mg, Part 1: Dose-Ranging Placebo 10 mg/Part 2: Bardoxolone Methyl 10 mg, Pa

| | |
|---|---|
| Comparison groups | Part 1:Dose-Ranging Bardoxolone Methyl 10mg v Part 1:Dose-Ranging Bardoxolone Methyl 20mg v Part 1:Dose-Ranging Placebo 2.5mg v Part 1: Dose-Ranging Placebo 5 mg v Part 1: Dose-Ranging Placebo 10 mg v Part 1: Dose-Ranging Placebo 20 mg v Part 1: Dose Titration: Bardoxolone Methyl 10 mg v Part 1: Dose Titration: Placebo 10 mg v Part 1:Dose-Ranging Bardoxolone Methyl 5mg v Part 1:Dose Ranging Bardoxolone Methyl 2.5mg |
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| P-value | = 0.8133 [4] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -1.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.22 |
| upper limit | 12.74 |

Notes:

[3] - Overall treatment effect in participants with PAH. Mean overall treatment effect across all visits for change from baseline in 6MWD was estimated and compared with placebo through 16 weeks of treatment using mixed-model repeated measures (MMRM), with treatment group, visit, and the interaction between treatment and visit as fixed factors. A compound symmetry covariance matrix was assumed. Data from Wks 4, 8, 12, and 16 used in the model with the change from baseline at Wk16 as primary endpoint.

[4] - The p-value comparison is for the difference in the change in 6WMD from baseline at Week 16 for bardoxolone methyl relative to placebo in participants with pulmonary arterial hypertension (PAH)

| Statistical analysis title | Statistical Analysis 2 |
|---|---|

Statistical analysis description:

Part 1: Dose Titration: Bardoxolone Methyl 10 mg/Part 2: Bardoxolone Methyl 10 mg, Part 1: Dose Titration: Placebo 10 mg/Part 2: Bardoxolone Methyl 10 mg

| | |
|---|---|
| Comparison groups | Part 1: Dose Titration: Bardoxolone Methyl 10 mg v Part 1: Dose Titration: Placebo 10 mg |
| Number of subjects included in analysis | 46 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[5] |
| P-value | = 0.759 [6] |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (net) |
| Point estimate | -3.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.54 |
| upper limit | 17.2 |

Notes:

[5] - Overall treatment effect in participants with PH. Mean overall treatment effect across all visits for change from baseline in 6MWD was estimated & compared with placebo through 16 wks of treatment using mixed-model repeated measures (MMRM), with treatment group, visit, and the interaction between treatment & visit as fixed factors. Compound symmetry covariance matrix was assumed. Data from Wks 4, 8, 12, and 16 were used in the model with the change from baseline at Wk 16 as the primary endpoint

[6] - The p-value comparison is for the difference in the change in 6WMD from baseline at Week 16 for bardoxolone methyl relative to placebo in participants with pulmonary hypertension (PH)

## Adverse events information

Timeframe for reporting adverse events:

Part 1: 16-week double-blind, randomized, placebo-controlled treatment period (Day 1 to Week 16).
Part 2: Open-label extension period (Week 16 onwards). Part 2 is the extension period, patients were to stay until study drug became available through EAP.

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

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 15 |

## Reporting groups

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 5 mg once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 2.5 mg once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 10 mg once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 20 mg once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 2.5 mg capsules once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 5 mg capsules once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 10 mg capsules once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl 10 mg capsules. Participants initially started with bardoxolone methyl 5 mg once-daily from Day 1 and titrated to bardoxolone methyl 10 mg once-daily starting at Week 4 up to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 20 mg capsules once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 1 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg |

Reporting group description:

Part 1: Participants were randomized to receive bardoxolone methyl matching placebo 10 mg capsules once-daily from Day 1 to Week 16.

| | |
|---|---|
| Reporting group title | Part 2 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label |

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 2.5 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 2.5 mg once-daily from Week 16 onwards.

| Reporting group title | Part 2 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label |
|---|---|

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 5 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 5 mg once-daily from Week 16 onwards.

| Reporting group title | Part 2 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label |
|---|---|

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 10 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 10 mg once-daily from Week 16 onwards.

| Reporting group title | Part 2 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label |
|---|---|

Reporting group description:

Part 2: Participants who completed treatment receiving bardoxolone methyl 20 mg once daily in Part 1 were eligible to continue to the extension Part 2 and continued to receive the same bardoxolone methyl 20 mg once-daily from Week 16 onwards.

| Reporting group title | Part 2 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg |
|---|---|

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 2.5 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 2.5 mg once-daily from Week 16 and onwards.

| Reporting group title | Part 2 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg |
|---|---|

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 5 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 5 mg once-daily from Week 16 and onwards.

| Reporting group title | Part 2 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg |
|---|---|

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 10 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.

| Reporting group title | Part 2 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg |
|---|---|

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 20 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 20 mg once-daily from Week 16 and onwards.

| Reporting group title | Part 2 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg |
|---|---|

Reporting group description:

Part 2: Participants who completed treatment titrated to 10 mg bardoxolone methyl in Part 1 were eligible to continue to the extension Part 2 and received bardoxolone methyl 10 mg once-daily from Week 16 and onwards.

| Reporting group title | Part 2 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg |
|---|---|

Reporting group description:

Part 2: Participants who completed bardoxolone methyl matching placebo 10 mg capsules once-daily treatment in Part 1 were eligible to continue to the extension Part 2 and initially received bardoxolone methyl 5 mg once-daily from Week 16 thru Week 20 and bardoxolone methyl 10 mg from Week 20 and onwards.

| **Serious adverse events** | Part 1 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label | Part 1 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label | Part 1 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Haemorrhagic ovarian cyst | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute right ventricular failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Part 1 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label | Part 1 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg | Part 1 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Delirium | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute right ventricular failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Part 1 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg | Part 1 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg | Part 1 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 7 / 74 (9.46%) | 1 / 4 (25.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute right ventricular failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Part 1 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg | Part 2 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label | Part 2 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 2 / 5 (40.00%) | 5 / 11 (45.45%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute right ventricular failure | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Blood and lymphatic system disorders** | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Gastrointestinal disorders** | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Part 2 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label | Part 2 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label | Part 2 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 6 / 9 (66.67%) | 0 / 1 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute right ventricular failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Part 2 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg | Part 2 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg | Part 2 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 3 (66.67%) | 1 / 3 (33.33%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute right ventricular failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Blood and lymphatic system disorders** | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Gastrointestinal disorders** | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salpingitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Part 2 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg | Part 2 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 63 (14.29%) | 9 / 33 (27.27%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Raynaud's phenomenon | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Delirium | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (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 | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (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 right ventricular failure | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac tamponade | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Right ventricular failure | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salpingitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fluid overload | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 2 %

| **Non-serious adverse events** | Part 1 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label | Part 1 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label | Part 1 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 12 (91.67%) | 5 / 6 (83.33%) | 10 / 11 (90.91%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|---|---|---|
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Asthenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 1 |
| Oedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 3 | 0 | 1 |
| Pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site swelling | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Social circumstances | | | |
| Menopause | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast mass | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vaginal disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 6 (16.67%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 1 | 2 |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 6 (16.67%) | 3 / 11 (27.27%) |
| occurrences (all) | 2 | 1 | 3 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epistaxis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 6 (16.67%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 1 | 1 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal septum perforation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngeal lesion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary congestion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinalgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Attention deficit/hyperactivity disorder | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac output increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous pressure jugular increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| White blood cell count increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Radius fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac discomfort | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericarditis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postural orthostatic tachycardia syndrome | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Dizziness exertional | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 6 (0.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 2 | 0 | 3 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Multiple sclerosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Occipital neuralgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital oedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleral disorder | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 0 | 2 |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colonic polyp | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 6 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 2 | 0 | 2 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Oesophageal spasm | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Painful defaecation | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Salivary gland enlargement | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 2 | 0 | 1 |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Digital ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |

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| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Subcutaneous nodule | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Urinary retention | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 6 (16.67%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 1 | 1 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Clubbing | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Exostosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fibromyalgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot deformity | | | |

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| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 3 / 11 (27.27%) |
| occurrences (all) | 0 | 1 | 3 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 2 | 0 | 1 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Plantar fasciitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctivitis infective | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Ear infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infected cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Lung infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 2 / 6 (33.33%) | 2 / 11 (18.18%) |
| occurrences (all) | 2 | 2 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 6 (16.67%) | 3 / 11 (27.27%) |
| occurrences (all) | 0 | 1 | 3 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Fluid retention | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Folate deficiency | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperalbuminaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 6 (16.67%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 6 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Part 1 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label | Part 1 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg | Part 1 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 12 (100.00%) | 2 / 2 (100.00%) | 4 / 4 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| **General disorders and administration site conditions** | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Oedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vessel puncture site swelling | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Social circumstances | | | |
| Menopause | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast mass | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea exertional | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasal septum perforation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Pharyngeal lesion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinalgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Anxiety | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac output increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous pressure jugular increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Weight increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pericardial effusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postural orthostatic tachycardia syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dizziness exertional | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 1 / 2 (50.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 5 | 1 | 1 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Multiple sclerosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Occipital neuralgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Tremor | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tympanic membrane perforation | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital oedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleral disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colonic polyp | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Frequent bowel movements | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 4 / 12 (33.33%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 4 | 0 | 1 |
| Oesophageal spasm | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Painful defaecation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary gland enlargement | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder polyp | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Digital ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash generalised | | | |

| | | | |
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| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous nodule | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 2 (50.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 1 | 1 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clubbing | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exostosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fibromyalgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Pain in jaw | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Conjunctivitis infective | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infected cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Sinusitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fluid retention | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folate deficiency | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperalbuminaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin B12 deficiency | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Part 1 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg | Part 1 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg | Part 1 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 63 / 74 (85.14%) | 4 / 4 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 7 / 74 (9.46%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 7 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Oedema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Social circumstances | | | |
| Menopause | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast mass | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 74 (5.41%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 8 / 74 (10.81%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 8 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal septum perforation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Pharyngeal lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Rhinalgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wheezing | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 5 / 74 (6.76%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 74 (5.41%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac output increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Venous pressure jugular increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vital capacity abnormal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 0 | 2 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac discomfort | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postural orthostatic tachycardia syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 74 (5.41%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 4 | 1 |
| Dizziness exertional | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 8 / 74 (10.81%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 8 | 1 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Multiple sclerosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Occipital neuralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Spinal claudication | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Syncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness bilateral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Periorbital oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleral disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 74 (1.35%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 1 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 74 (5.41%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colonic polyp | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 10 / 74 (13.51%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 10 | 0 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 5 / 74 (6.76%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower gastrointestinal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 10 / 74 (13.51%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 10 | 0 |
| Oesophageal spasm | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Painful defaecation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary gland enlargement | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Digital ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Psoriasis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous nodule | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Dysuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 74 (4.05%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 74 (5.41%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clubbing | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exostosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fibromyalgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 11 / 74 (14.86%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 11 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Neck pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis infective | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infected cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 7 / 74 (9.46%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 7 | 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 74 (5.41%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 74 (2.70%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 10 / 74 (13.51%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 10 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 5 / 74 (6.76%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 5 | 1 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 7 / 74 (9.46%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 7 | 0 |
| Dyslipidaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Fluid retention | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Folate deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 74 (1.35%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperalbuminaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactose intolerance | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 74 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Part 1 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg | Part 2 of Part 1: Dose-Ranging BM 2.5 mg/Part 2: Open-Label | Part 2 of Part 1: Dose-Ranging BM 5 mg/Part 2: Open-Label |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 38 (86.84%) | 5 / 5 (100.00%) | 11 / 11 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Hypertension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 5 / 38 (13.16%) | 2 / 5 (40.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 5 | 2 | 3 |
| Pain | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site swelling | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Social circumstances | | | |
| Menopause | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Breast mass | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal disorder | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchial hyperreactivity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 4 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 5 (20.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 1 | 2 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal septum perforation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Pharyngeal lesion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinalgia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Sleep apnoea syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 5 (20.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 1 | 1 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac output increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 1 / 5 (20.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 2 | 1 | 2 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous pressure jugular increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial flutter | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac discomfort | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 1 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postural orthostatic tachycardia syndrome | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Central nervous system lesion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 1 / 5 (20.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 3 | 1 | 1 |
| Dizziness exertional | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 7 / 38 (18.42%) | 3 / 5 (60.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 7 | 3 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Multiple sclerosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Occipital neuralgia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Somnolence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 1 |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital oedema | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Retinal tear | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Scleral disorder | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Vision blurred | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 0 | 0 | 3 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Colonic polyp | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 1 / 5 (20.00%) | 3 / 11 (27.27%) |
| occurrences (all) | 3 | 1 | 3 |
| Dental caries | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 2 / 5 (40.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 3 | 2 | 2 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Duodenitis | | | |

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| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Lip dry | | | |

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| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 6 / 38 (15.79%) | 3 / 5 (60.00%) | 4 / 11 (36.36%) |
| occurrences (all) | 6 | 3 | 4 |
| Oesophageal spasm | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Painful defaecation | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary gland enlargement | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Toothache | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 5 (40.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Digital ulcer | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 1 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin haemorrhage | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Subcutaneous nodule | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 5 (40.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 4 / 38 (10.53%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 4 | 0 | 1 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chondrocalcinosis pyrophosphate | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clubbing | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exostosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Fibromyalgia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 2 | 0 | 1 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 5 (40.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 2 / 5 (40.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 2 / 5 (40.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 2 | 1 |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Cellulitis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Clostridial infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis infective | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 5 (20.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 1 | 2 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Infected cyst | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 38 (7.89%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 1 | 0 | 2 |

| | | | |
|---|---|---|---|
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 1 | 1 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 38 (18.42%) | 2 / 5 (40.00%) | 4 / 11 (36.36%) |
| occurrences (all) | 7 | 2 | 4 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 38 (2.63%) | 1 / 5 (20.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 1 | 1 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 1 / 5 (20.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fluid overload | | | |
| subjects affected / exposed | 2 / 38 (5.26%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Fluid retention | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Folate deficiency | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Gout | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperalbuminaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 2 / 5 (40.00%) | 2 / 11 (18.18%) |
| occurrences (all) | 0 | 2 | 2 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |
| Lactic acidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 0 / 11 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 38 (0.00%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 1 / 38 (2.63%) | 0 / 5 (0.00%) | 1 / 11 (9.09%) |
| occurrences (all) | 1 | 0 | 1 |

| **Non-serious adverse events** | Part 2 of Part 1: Dose-Ranging BM 10 mg/Part 2: Open-Label | Part 2 of Part 1: Dose-Ranging BM 20 mg/Part 2: Open-Label | Part 2 of Part 1: Dose-Ranging Pbo 2.5 mg/Part 2: BM 2.5 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 6 (100.00%) | 8 / 9 (88.89%) | 1 / 1 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Hot flush | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 6 (50.00%) | 1 / 9 (11.11%) | 1 / 1 (100.00%) |
| occurrences (all) | 3 | 1 | 1 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site swelling | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Social circumstances | | | |
| Menopause | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast mass | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 4 / 6 (66.67%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal septum perforation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pharyngeal lesion | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinalgia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac output increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Venous pressure jugular increased | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ligament sprain | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Radius fracture | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial flutter | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac discomfort | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postural orthostatic tachycardia syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Central nervous system lesion | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 9 (11.11%) | 1 / 1 (100.00%) |
| occurrences (all) | 1 | 1 | 1 |
| Dizziness exertional | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Multiple sclerosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Occipital neuralgia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |

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| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Meniere's disease | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital oedema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleral disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Vision blurred | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colonic polyp | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 9 (22.22%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 1 / 1 (100.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |

| | | | |
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| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oesophageal spasm | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Painful defaecation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary gland enlargement | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 9 (22.22%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
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| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Digital ulcer | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin haemorrhage | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Subcutaneous nodule | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chondrocalcinosis pyrophosphate | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clubbing | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exostosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fibromyalgia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 9 (22.22%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis infective | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Infected cyst | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 9 (22.22%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|---|---|---|---|
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 9 (22.22%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Fluid retention | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Folate deficiency | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperalbuminaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 2 / 9 (22.22%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lactic acidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 9 (11.11%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 9 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Part 2 of Part 1: Dose-Ranging Pbo 5 mg/Part 2: BM 5 mg | Part 2 of Part 1: Dose-Ranging Pbo 10 mg/Part 2: BM 10 mg | Part 2 of Part 1: Dose-Ranging Pbo 20 mg/Part 2: BM 20 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 3 / 3 (100.00%) | 3 / 3 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Hot flush | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vessel puncture site swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Social circumstances | | | |
| Menopause | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasal septum perforation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pharyngeal lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinalgia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac output increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous pressure jugular increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Atrial flutter | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postural orthostatic tachycardia syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Central nervous system lesion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness exertional | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 3 (66.67%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Multiple sclerosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Occipital neuralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleral disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Vision blurred | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colonic polyp | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Oesophageal spasm | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Painful defaecation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary gland enlargement | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Digital ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous nodule | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 3 (66.67%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chondrocalcinosis pyrophosphate | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clubbing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exostosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fibromyalgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 3 (66.67%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis infective | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Infected cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 3 (66.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyslipidaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fluid retention | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folate deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperalbuminaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactic acidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Part 2 of Part 1: Dose Titration: BM 10 mg/Part 2: BM 10 mg | Part 2 of Part 1: Dose Titration: Pbo 10 mg/Part 2: BM 10 mg | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 47 / 63 (74.60%) | 30 / 33 (90.91%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Hot flush | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 33 (6.06%) | |
| occurrences (all) | 0 | 2 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Chills | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 4 / 33 (12.12%) | |
| occurrences (all) | 4 | 4 | |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Implant site haematoma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Irritability | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 0 / 33 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Oedema | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 3 / 33 (9.09%) | |
| occurrences (all) | 4 | 3 | |
| Pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 33 (6.06%) | |
| occurrences (all) | 0 | 2 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 33 (6.06%) | |
| occurrences (all) | 0 | 2 | |
| Vessel puncture site haematoma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vessel puncture site pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vessel puncture site swelling | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Social circumstances | | | |
| Menopause | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Breast mass | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vaginal disorder | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cough | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 4 / 33 (12.12%) | |
| occurrences (all) | 5 | 4 | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 4 / 33 (12.12%) | |
| occurrences (all) | 5 | 4 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dyspnoea paroxysmal nocturnal | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 3 / 33 (9.09%) | |
| occurrences (all) | 0 | 3 | |
| Nasal dryness | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nasal septum perforation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 33 (6.06%) | |
| occurrences (all) | 1 | 2 | |
| Pharyngeal lesion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Productive cough | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 1 / 33 (3.03%) | |
| occurrences (all) | 3 | 1 | |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Rales | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Rhinalgia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinus congestion | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Wheezing | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Depression | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Hallucination | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 33 (6.06%) | |
| occurrences (all) | 1 | 2 | |
| Aspartate aminotransferase increased | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | | |
| occurrences (all) | 1 | 1 | | |
| Blood bicarbonate decreased | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | | |
| occurrences (all) | 0 | 1 | | |
| Blood bilirubin increased | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Blood creatine phosphokinase increased | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Blood creatinine increased | | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 2 | 0 | | |
| Blood phosphorus decreased | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Blood potassium decreased | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Blood urine present | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Brain natriuretic peptide increased | | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 3 / 33 (9.09%) | | |
| occurrences (all) | 3 | 3 | | |
| Cardiac murmur | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Cardiac output increased | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Electrocardiogram QT prolonged | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |

| | | | |
|---|---|---|---|
| Electrocardiogram abnormal | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Liver function test abnormal | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 33 (6.06%) | |
| occurrences (all) | 1 | 2 | |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 2 / 33 (6.06%) | |
| occurrences (all) | 4 | 2 | |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pulmonary arterial pressure increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Venous pressure jugular increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 63 (3.17%) | 0 / 33 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 33 (6.06%) | |
| occurrences (all) | 1 | 2 | |
| Weight increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| White blood cell count increased | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 0 / 33 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Joint injury | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Laceration | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 0 / 33 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Ligament sprain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 63 (3.17%) | 0 / 33 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Limb injury | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Atrial flutter | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac discomfort | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 0 / 33 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Postural orthostatic tachycardia syndrome | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Central nervous system lesion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dizziness exertional | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Headache | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 3 / 33 (9.09%) | |
| occurrences (all) | 2 | 3 | |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Migraine | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Multiple sclerosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Occipital neuralgia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Somnolence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Spinal claudication | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Tremor | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 0 / 33 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Coagulopathy | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Splenic vein thrombosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Keratitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Periorbital oedema | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Retinal tear | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Scleral disorder | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Vision blurred | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 2 / 33 (6.06%) | |
| occurrences (all) | 3 | 2 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Colonic polyp | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Constipation | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 1 / 33 (3.03%) | |
| occurrences (all) | 4 | 1 | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 7 / 33 (21.21%) | |
| occurrences (all) | 1 | 7 | |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Duodenitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Frequent bowel movements | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 33 (6.06%) | |
| occurrences (all) | 1 | 2 | |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lip dry | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 3 / 33 (9.09%) | |
| occurrences (all) | 2 | 3 | |
| Oesophageal spasm | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Painful defaecation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 33 (6.06%) | |
| occurrences (all) | 0 | 2 | |
| Retching | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Salivary gland enlargement | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Toothache | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Gallbladder polyp | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermal cyst | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Digital ulcer | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Erythema | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pruritus | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rash papular | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin haemorrhage | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin irritation | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Subcutaneous nodule | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 0 / 33 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Arthropathy | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Bone pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Bursitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Chondrocalcinosis pyrophosphate | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Clubbing | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Exostosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Fibromyalgia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Muscle spasms | | | |
| subjects affected / exposed | 5 / 63 (7.94%) | 5 / 33 (15.15%) | |
| occurrences (all) | 5 | 5 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Myalgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 1 / 33 (3.03%) | |
| occurrences (all) | 3 | 1 | |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Plantar fasciitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Scleroderma | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Temporomandibular joint syndrome | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Breast abscess | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Candidiasis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Cellulitis | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 0 / 33 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Clostridial infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Conjunctivitis infective | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ear infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 33 (6.06%) | |
| occurrences (all) | 0 | 2 | |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Helicobacter infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| Infected cyst | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 33 (6.06%) | |
| occurrences (all) | 0 | 2 | |
| Lung infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 33 (6.06%) | |
| occurrences (all) | 1 | 2 | |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | |
| occurrences (all) | 0 | 1 | |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 1 / 33 (3.03%) | |
| occurrences (all) | 2 | 1 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |

| | | | |
|---|---|---|---|
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 2 / 33 (6.06%) | |
| occurrences (all) | 1 | 2 | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 2 / 33 (6.06%) | |
| occurrences (all) | 4 | 2 | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | |
| occurrences (all) | 1 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 12 / 63 (19.05%) | 9 / 33 (27.27%) | |
| occurrences (all) | 12 | 9 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 63 (6.35%) | 2 / 33 (6.06%) | |
| occurrences (all) | 4 | 2 | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vulvovaginal mycotic infection | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 3 / 63 (4.76%) | 6 / 33 (18.18%) | | |
| occurrences (all) | 3 | 6 | | |
| Dyslipidaemia | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Fluid overload | | | | |
| subjects affected / exposed | 3 / 63 (4.76%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 3 | 0 | | |
| Fluid retention | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | | |
| occurrences (all) | 0 | 1 | | |
| Folate deficiency | | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | | |
| occurrences (all) | 1 | 1 | | |
| Glucose tolerance impaired | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Gout | | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Hyperalbuminaemia | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Hypercholesterolaemia | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 33 (3.03%) | | |
| occurrences (all) | 0 | 1 | | |
| Hypokalaemia | | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 1 / 33 (3.03%) | | |
| occurrences (all) | 1 | 1 | | |
| Hypomagnesaemia | | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 33 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Iron deficiency | | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 33 (6.06%) | | |
| occurrences (all) | 0 | 2 | | |
| Lactic acidosis | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lactose intolerance | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 0 / 33 (0.00%) | |
| occurrences (all) | 0 | 0 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 29 October 2013 | Protocol Version 1.0 (No patients were enrolled under protocol version 1.0) |
| 05 December 2013 | Protocol Version 2.0 |
| 20 August 2014 | Protocol Version 3.0 |
| 24 November 2014 | Protocol Version 4.0 |
| 31 August 2015 | Protocol Version 5.0 |
| 01 June 2016 | Protocol Version 6.0 |
| 26 January 2017 | Protocol Version 7.0 |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported