Clinical trial results:
26-Week Randomized, Double-Blinded, Active Controlled Study Comparing the Safety of Mometasone Furoate/Formoterol Fumarate MDI Fixed Dose Combination Versus Mometasone Furoate MDI Monotherapy in Adolescents and Adults With Persistent Asthma

Summary

EudraCT number	2011-002142-13
Trial protocol	HU EE CZ LV GB ES DE IE SK PL IT BG Outside EU/EEA
Global end of trial date	30 November 2016

Results information

Result version number	v1 (current)
This version publication date	09 July 2017
First version publication date	09 July 2017

Trial information

Trial identification

Sponsor protocol code	P202 (also known as P06241)

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01471340
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2016
Global end of trial reached?	Yes
Global end of trial date	30 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare serious asthma outcomes (a composite endpoint defined as asthma-related: hospitalizations, intubations and deaths) in participants treated with mometasone furoate/formoterol fumarate (MF/F) versus participants treated with mometasone furoate (MF), each administered by a metered-dose inhaler (MDI), twice daily (BID), and assessed by a non-inferiority test.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human participants participating in biomedical research. The following additional measure(s) defined for this study were provided for protection of trial participants: albuterol/salbutamol hydrofluoroalkane (HFA) MDI administered as needed as rescue medication; systemic corticosteroids (tablets, suspension, or injection) were provided only as an emergency rescue medication at the discretion of the investigator.

Background therapy:

Placebo MDIs were provided for on-site training on inhaler use.

Evidence for comparator: -

Actual start date of recruitment	09 January 2012
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	Argentina: 360
Country: Number of subjects enrolled	Australia: 43
Country: Number of subjects enrolled	Brazil: 274
Country: Number of subjects enrolled	Bulgaria: 510
Country: Number of subjects enrolled	Canada: 201
Country: Number of subjects enrolled	Chile: 217
Country: Number of subjects enrolled	China: 169
Country: Number of subjects enrolled	Colombia: 215
Country: Number of subjects enrolled	Croatia: 83
Country: Number of subjects enrolled	Czech Republic: 438
Country: Number of subjects enrolled	Estonia: 60
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Germany: 152
Country: Number of subjects enrolled	Guatemala: 209
Country: Number of subjects enrolled	Hungary: 134

Country: Number of subjects enrolled	Ireland: 51
Country: Number of subjects enrolled	Israel: 29
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Korea, Republic of: 90
Country: Number of subjects enrolled	Latvia: 520
Country: Number of subjects enrolled	Malaysia: 123
Country: Number of subjects enrolled	Mexico: 396
Country: Number of subjects enrolled	Peru: 528
Country: Number of subjects enrolled	Poland: 622
Country: Number of subjects enrolled	Puerto Rico: 42
Country: Number of subjects enrolled	Romania: 461
Country: Number of subjects enrolled	Russian Federation: 535
Country: Number of subjects enrolled	Serbia: 684
Country: Number of subjects enrolled	Slovakia: 202
Country: Number of subjects enrolled	South Africa: 369
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Taiwan: 61
Country: Number of subjects enrolled	Ukraine: 1234
Country: Number of subjects enrolled	United Kingdom: 253
Country: Number of subjects enrolled	United States: 2412
Worldwide total number of subjects	11729
EEA total number of subjects	3538

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)	1037
Adults (18-64 years)	9094
From 65 to 84 years	1588
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

Participants (either sex, any race, >= 12 yr of age) had a diagnosis of asthma for at least 1 yr, used daily asthma controller medication for at least 4 wk prior to randomisation and had a history of at least one asthma exacerbation requiring hospitalisation or systemic corticosteroid in the previous year (excluding the 4 wk before randomisation).

Pre-assignment

Screening details:

During a screening period that lasted up to 2 weeks, all participants remained on their incoming asthma medication.

Period 1

Period 1 title	Randomised Participants
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	MF/F MDI BID

Arm description:

MF/F MDI, administered as 200/10 mcg BID or 400/10 mcg BID

Arm type	Experimental
Investigational medicinal product name	MF/F MDI
Investigational medicinal product code	MK-0887A
Other name	DULERA / ZENHALE
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

MF/F MDI administered as two puffs of 100/5 mcg or 200/5 mcg, twice daily, with oral inhalation of a pressurized inhalation aerosol

Investigational medicinal product name	Oral prednisone or prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral prednisone or prednisolone for acute administration as emergency rescue medication at the discretion
of the investigator

Investigational medicinal product name	Albuterol/Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

Albuterol 90 mcg HFA MDI/Salbutamol 100 mcg HFA MDI for as needed asthma symptom relief

Arm title	MF MDI BID

Arm description:

MF MDI, administered as 200 mcg BID or 400 mcg BID

Arm type	Active comparator
Investigational medicinal product name	MF MDI
Investigational medicinal product code	
Other name	ASMANEX
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

MF MDI administered as two puffs of 100 mcg or 200 mcg, twice daily, with oral inhalation of a pressurized inhalation aerosol

Investigational medicinal product name	Oral prednisone or prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral prednisone or prednisolone for acute administration as emergency rescue medication at the discretion
of the investigator

Investigational medicinal product name	Albuterol/Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use

Dosage and administration details:

Albuterol 90 mcg HFA MDI/Salbutamol 100 mcg HFA MDI for as needed asthma symptom relief

Number of subjects in period 1	MF/F MDI BID	MF MDI BID
Started	5868	5861
Completed	5868	5861

Period 2

Period 2 title	Treatment, Including Safety Follow-Up
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Arms

Are arms mutually exclusive?	Yes

Arm title	MF/F MDI BID
Arm description:	
MF/F MDI, administered as 200/10 mcg BID or 400/10 mcg BID	
Arm type	Experimental
Investigational medicinal product name	MF/F MDI
Investigational medicinal product code	MK-0887A
Other name	DULERA / ZENHALE
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use
Dosage and administration details:	
MF/F MDI administered as two puffs of 100/5 mcg or 200/5 mcg, twice daily, with oral inhalation of a pressurized inhalation aerosol	
Investigational medicinal product name	Albuterol/Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use
Dosage and administration details:	
Albuterol 90 mcg HFA MDI/Salbutamol 100 mcg HFA MDI for as needed asthma symptom relief	
Investigational medicinal product name	Oral prednisone or prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Oral prednisone or prednisolone for acute administration as emergency rescue medication at the discretion of the investigator	
Arm title	MF MDI BID
Arm description:	
MF MDI, administered as 200 mcg BID or 400 mcg BID	
Arm type	Active comparator
Investigational medicinal product name	MF MDI
Investigational medicinal product code	MK-0887
Other name	DULERA / ZENHALE
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use
Dosage and administration details:	
MF MDI administered as two puffs of 100 mcg or 200 mcg, twice daily, with oral inhalation of a pressurized inhalation aerosol	
Investigational medicinal product name	Albuterol/Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pressurised inhalation
Routes of administration	Inhalation use
Dosage and administration details:	
Albuterol 90 mcg HFA MDI/Salbutamol 100 mcg HFA MDI for as needed asthma symptom relief	
Investigational medicinal product name	Oral prednisone or prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Oral prednisone or prednisolone for acute administration as emergency rescue medication at the discretion
of the investigator

Number of subjects in period 2	MF/F MDI BID	MF MDI BID
Started	5868	5861
Completed	5862	5855
Not completed	6	6
Death	5	4
Study terminated by sponsor	1	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	MF/F MDI BID
Reporting group description:	
MF/F MDI, administered as 200/10 mcg BID or 400/10 mcg BID	
Reporting group title	MF MDI BID
Reporting group description:	
MF MDI, administered as 200 mcg BID or 400 mcg BID	

Reporting group values	MF/F MDI BID	MF MDI BID	Total
Number of subjects	5868	5861	11729
Age Categorical			
Three participants with a calculated age of less than 12 years are included in the adolescent subgroup. One participant was less than 2 weeks under the age of 12 at the time of randomisation. Two other participants were at least 12 years of age at the time of randomisation.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	491	546	1037
Adults (18-64 years)	4578	4516	9094
From 65-84 years	797	791	1588
85 years and over	2	8	10
Age Continuous			
Age of randomized participants at baseline			
Units: years			
arithmetic mean	45.3	44.8	
standard deviation	± 17.2	± 17.6	-
Gender Categorical			
Units: Subjects			
Female	3841	3875	7716
Male	2027	1986	4013

Subject analysis sets	
Subject analysis set title	MF/F MDI BID
Subject analysis set type	Full analysis
Subject analysis set description:	
MF/F MDI administered as 200/10 mcg BID or 400/10 mcg BID	
Subject analysis set title	MF MDI BID
Subject analysis set type	Full analysis
Subject analysis set description:	
MF MDI administered as 200 mcg BID or 400 mcg BID	

Reporting group values	MF/F MDI BID	MF MDI BID	
Number of subjects	5868	5861	
Age Categorical			
Three participants with a calculated age of less than 12 years are included in the adolescent subgroup. One participant was less than 2 weeks under the age of 12 at the time of randomisation. Two other participants were at least 12 years of age at the time of randomisation.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	491	546	
Adults (18-64 years)	4578	4516	
From 65-84 years	797	791	
85 years and over	2	8	
Age Continuous			
Age of randomized participants at baseline			
Units: years			
arithmetic mean	45.3	44.8	
standard deviation	± 17.2	± 17.6	
Gender Categorical			
Units: Subjects			
Female	3841	3875	
Male	2027	1986	

End points

End points reporting groups

Reporting group title	MF/F MDI BID
Reporting group description: MF/F MDI, administered as 200/10 mcg BID or 400/10 mcg BID	
Reporting group title	MF MDI BID
Reporting group description: MF MDI, administered as 200 mcg BID or 400 mcg BID	
Reporting group title	MF/F MDI BID
Reporting group description: MF/F MDI, administered as 200/10 mcg BID or 400/10 mcg BID	
Reporting group title	MF MDI BID
Reporting group description: MF MDI, administered as 200 mcg BID or 400 mcg BID	
Subject analysis set title	MF/F MDI BID
Subject analysis set type	Full analysis
Subject analysis set description: MF/F MDI administered as 200/10 mcg BID or 400/10 mcg BID	
Subject analysis set title	MF MDI BID
Subject analysis set type	Full analysis
Subject analysis set description: MF MDI administered as 200 mcg BID or 400 mcg BID	

Primary: Time-to-First Serious Asthma Outcomes (SAO: Composite of Asthma-Related Hospitalisations, Asthma-Related Intubations, and Asthma-Related Deaths) in MF/F Participants vs MF Participants

End point title	Time-to-First Serious Asthma Outcomes (SAO: Composite of Asthma-Related Hospitalisations, Asthma-Related Intubations, and Asthma-Related Deaths) in MF/F Participants vs MF Participants

End point description:

The primary safety endpoint was the time-to-first SAO (a composite endpoint of asthma-related hospitalisations, asthma-related intubations, and asthma-related deaths) in participants treated with MF/F MDI BID versus participants treated with MF MDI BID. The time-to-first SAO was assessed by a non-inferiority test, in which the criteria for non-inferiority were defined by the upper bound limit of 2.0 for the 95% confidence interval of the hazard ratio (HR) of MF/F MDI BID to MF MDI BID. The analysed population for assessment of time-to-first SAO was all participants who received at least one dose of randomised treatment assignment (intention-to-treat principle).

End point type	Primary

End point timeframe:

Up to 26 weeks, or 7 days after the last treatment dose, whichever occurred later

End point values	MF/F MDI BID	MF MDI BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5868	5861		
Units: Number of participants				
number (not applicable)				
Total Number of SAO	39	32		

Statistical analyses

Statistical analysis title	Difference in Time-to-First SAO

Statistical analysis description:

For analysis of the time-to-first SAO, MF/F MDI BID was considered non-inferior to MF MDI BID if the upper bound of the two-sided 95% confidence interval (CI) of the hazard ratio (HR) of MF/F MDI BID versus MF MDI BID was lower than 2.0 (noninferiority margin).

Comparison groups	MF/F MDI BID v MF MDI BID
Number of subjects included in analysis	11729
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	Cox proportional-hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.94

Notes:

[1] - The HR and 95% CI were based on the Cox proportional-hazard model with covariates of treatment (MF/F or MF) and ICS dose level (200 or 400 mcg).

Secondary: Time-to-First Asthma Exacerbation in MF/F Participants vs MF Participants

End point title	Time-to-First Asthma Exacerbation in MF/F Participants vs MF Participants

End point description:

A key secondary efficacy endpoint was the time-to-first protocol-defined asthma exacerbation (SAEX). The SAEX were deteriorations of asthma requiring: the use of systemic corticosteroids (tablets, suspension, or injection) for at least 3 consecutive days, an in-patient hospitalisation, or an ED visit less than 24 hours that required systemic corticosteroids in participants treated with MF/F MDI BID versus participants treated with MF MDI BID. Superiority of MF/F MDI BID was determined if the HR of MF/F MDI BID to MF MDI BID is less than 1 and achieved statistical significance (one sided p-value < 0.025). The analysed population for assessment of time-to-first asthma exacerbation was all treated participants who received at least one dose of randomised treatment assignment (intention-to-treat principle).

End point type	Secondary

End point timeframe:

Up to 26 weeks, or 7 days after the last treatment dose, whichever occurred later

End point values	MF/F MDI BID	MF MDI BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5868	5861		
Units: First SAEX				
Number of Participants with First SAEX	708	779		

Statistical analyses

Statistical analysis title	Difference in Time-to-First Exacerbation

Statistical analysis description:

Superiority of MF/F MDI BID was determined if the HR of MF/F MDI BID to MF MDI BID was less than 1 and achieved statistical significance (one-sided p-value < 0.025).

Comparison groups	MF/F MDI BID v MF MDI BID
Number of subjects included in analysis	11729
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.021
Method	Cox proportional-hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	0.98

Notes:

[2] - The HR and 95% CI were based on the Cox proportional-hazard model with covariates of treatment (MF/F or MF) and ICS dose level (200 or 400 mcg).

Other pre-specified: Number of SAO Components in MF/F Participants vs MF Participants

End point title	Number of SAO Components in MF/F Participants vs MF Participants

End point description:

To further examine the primary safety endpoint, each component of the SAO composite (asthma-related hospitalisations, asthma-related intubations, and asthma-related deaths) was tabulated for descriptive purposes only to show the relative contribution of each component to the SAO composite. Hospitalisation was defined as an inpatient stay or >= 24 hour stay in an observational area in an emergency department or equivalent healthcare facility. Intubation was defined as endotracheal intubation only. The analysed population for tabulation of time-to-first SAO components was all participants who received at least one dose of randomised treatment assignment (intention-to-treat principle).

End point type	Other pre-specified

End point timeframe:

Up to 26 weeks, or 7 days after the last treatment dose, whichever occurred later

End point values	MF/F MDI BID	MF MDI BID		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5868	5861		
Units: Number of participants				
First SAO	39	32		
Asthma-related hospitalisations	39	32		
Asthma-related intubations	0	0		
Asthma-related deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 26 weeks, or 7 days after the last treatment dose, whichever occurred later

Adverse event reporting additional description:

The safety analysis set was defined as all participants who received at least one dose of randomised treatment assignment (intention-to-treat principle). Non-serious AEs were only collected for participants who discontinued treatment due to an AE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	MF/F MDI BID
Reporting group description: -	
Reporting group title	MF MDI BID

Reporting group description: -

Serious adverse events	MF/F MDI BID	MF MDI BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	136 / 5868 (2.32%)	137 / 5861 (2.34%)	
number of deaths (all causes)	5	4	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of spinal cord			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid tumour of the duodenum			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			

subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medullary thyroid cancer			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			

subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	3 / 5868 (0.05%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion incomplete			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion missed			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abortion spontaneous			
subjects affected / exposed	2 / 5868 (0.03%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ectopic pregnancy			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foetal death			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (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			
Chest pain			
subjects affected / exposed	2 / 5868 (0.03%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Non-cardiac chest pain			
subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Fibrocystic breast disease			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postmenopausal haemorrhage			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicocele			

subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	32 / 5868 (0.55%)	31 / 5861 (0.53%)	
occurrences causally related to treatment / all	0 / 34	0 / 34	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiectasis			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			

subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 5868 (0.05%)	4 / 5861 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary oedema			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			

subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol abuse			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Depression			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophreniform disorder			

subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Chest X-ray abnormal			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (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			
Accidental overdose			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 5868 (0.02%)	4 / 5861 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns third degree			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Head injury			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional product misuse			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			

subjects affected / exposed	2 / 5868 (0.03%)	3 / 5861 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hypertrophic cardiomyopathy			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 5868 (0.02%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrioventricular block complete			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	3 / 5868 (0.05%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomegaly			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery thrombosis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diastolic dysfunction			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve stenosis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis autoimmune			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IIIrd nerve paralysis			

subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lacunar infarction			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylitic myelopathy			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 5868 (0.03%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukocytosis			

subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiploic appendagitis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric dysplasia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal necrosis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal sphincter insufficiency			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Biliary colic			
subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 5868 (0.02%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	2 / 5868 (0.03%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 5868 (0.02%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin hypertrophy			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			

subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 5868 (0.02%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basedow's disease			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthritis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondropathy			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint range of motion decreased			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			

subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess intestinal			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anicteric leptospirosis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	6 / 5868 (0.10%)	4 / 5861 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	3 / 5868 (0.05%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 5868 (0.05%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema infected			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (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	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis cryptococcal			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			

subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pilonidal cyst			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	10 / 5868 (0.17%)	6 / 5861 (0.10%)	
occurrences causally related to treatment / all	1 / 11	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia bacterial			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pseudomonal			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperosmolar state			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			

subjects affected / exposed	1 / 5868 (0.02%)	2 / 5861 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MF/F MDI BID	MF MDI BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 5868 (1.45%)	101 / 5861 (1.72%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hepatic cancer			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Ovarian adenoma			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			

subjects affected / exposed	1 / 5868 (0.02%)	3 / 5861 (0.05%)	
occurrences (all)	1	3	
Chest pain			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Feeling jittery			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Mucosal inflammation			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Immune system disorders			
Allergic oedema			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Drug hypersensitivity			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	8 / 5868 (0.14%)	10 / 5861 (0.17%)	
occurrences (all)	8	10	
Bronchospasm			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences (all)	0	2	
Bronchospasm paradoxical			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	2 / 5868 (0.03%)	6 / 5861 (0.10%)	
occurrences (all)	2	6	
Dysphonia			
subjects affected / exposed	4 / 5868 (0.07%)	5 / 5861 (0.09%)	
occurrences (all)	4	5	
Dyspnoea			
subjects affected / exposed	4 / 5868 (0.07%)	5 / 5861 (0.09%)	
occurrences (all)	4	5	
Hypopnoea			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Interstitial lung disease			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Laryngeal hypertrophy			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Laryngeal oedema			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Oropharyngeal pain			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences (all)	0	2	
Pulmonary embolism			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences (all)	0	2	
Respiratory tract congestion			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Throat irritation			

subjects affected / exposed	2 / 5868 (0.03%)	1 / 5861 (0.02%)	
occurrences (all)	2	1	
Vocal cord disorder			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 5868 (0.00%)	3 / 5861 (0.05%)	
occurrences (all)	0	3	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Completed suicide			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Insomnia			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Investigations			
Heart rate increased			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Myocardial infarction acute			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Angina pectoris			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	

Arrhythmia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Cardiac failure			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Cardiac failure congestive			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Cardiomegaly			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Coronary artery thrombosis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Myocardial infarction			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	2 / 5868 (0.03%)	1 / 5861 (0.02%)	
occurrences (all)	2	1	
Supraventricular tachycardia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences (all)	0	2	
Nervous system disorders			
Aphonia			

subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences (all)	0	2	
Dizziness			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Epilepsy			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	3 / 5868 (0.05%)	7 / 5861 (0.12%)	
occurrences (all)	3	7	
IIIrd nerve paralysis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Ischaemic stroke			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	2 / 5868 (0.03%)	1 / 5861 (0.02%)	
occurrences (all)	2	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	3 / 5868 (0.05%)	0 / 5861 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal necrosis			

subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Glossodynia			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Oral discomfort			
subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Oral mucosal erythema			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Retching			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	2 / 5868 (0.03%)	3 / 5861 (0.05%)	
occurrences (all)	2	3	
Tongue discomfort			
subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Angioedema			

subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Dermatitis acneiform			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Lichen planus			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Muscle spasms			

subjects affected / exposed	1 / 5868 (0.02%)	1 / 5861 (0.02%)	
occurrences (all)	1	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 5868 (0.00%)	2 / 5861 (0.03%)	
occurrences (all)	0	2	
Candida infection			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Laryngitis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Oral fungal infection			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	2 / 5868 (0.03%)	0 / 5861 (0.00%)	
occurrences (all)	2	0	

Pneumonia			
subjects affected / exposed	2 / 5868 (0.03%)	2 / 5861 (0.03%)	
occurrences (all)	2	2	
Sinusitis			
subjects affected / exposed	1 / 5868 (0.02%)	0 / 5861 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 5868 (0.00%)	3 / 5861 (0.05%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 5868 (0.00%)	1 / 5861 (0.02%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported