



Clinical trial results:

The Impact of LY2605541 versus Insulin Glargine for Patients with Type 2 Diabetes Mellitus Advanced to Multiple Injection Bolus Insulin with Insulin Lispro: a Double-Blind, Randomized, 26-week Study - The IMAGINE 4 Study

Summary

EudraCT number	2011-001254-29
Trial protocol	DE HU SK GB CZ AT ES LT GR IT DK NL SI
Global end of trial date	13 August 2013

Results information

Result version number	v1 (current)
This version publication date	02 April 2018
First version publication date	02 April 2018

Trial information

Trial identification

Sponsor protocol code	I2R-MC-BIAM
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01468987
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 12145

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	13 August 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 August 2013
Global end of trial reached?	Yes
Global end of trial date	13 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is:

- To compare blood glucose (blood sugar) control on LY2605541 with insulin glargine after 26 weeks of treatment.
- To compare the rate of night time hypoglycemia (low blood glucose) on LY2605541 with insulin glargine during 26 weeks of treatment.
- To compare the number of participants on LY2605541 reaching blood glucose targets without hypoglycemia episodes at night to those taking insulin glargine after 26 weeks of treatment.
- To compare the rate of hypoglycemia over a 24-hour period on LY2605541 with insulin glargine during 26 weeks of treatment.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2011
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: 546
Country: Number of subjects enrolled	Taiwan: 15
Country: Number of subjects enrolled	Slovakia: 42
Country: Number of subjects enrolled	Greece: 23
Country: Number of subjects enrolled	Spain: 65
Country: Number of subjects enrolled	Lithuania: 6
Country: Number of subjects enrolled	Turkey: 11
Country: Number of subjects enrolled	Austria: 15
Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	Israel: 40
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Italy: 32
Country: Number of subjects enrolled	Czech Republic: 45
Country: Number of subjects enrolled	Hungary: 72
Country: Number of subjects enrolled	Mexico: 25

Country: Number of subjects enrolled	Puerto Rico: 46
Country: Number of subjects enrolled	Poland: 40
Country: Number of subjects enrolled	Brazil: 24
Country: Number of subjects enrolled	Romania: 65
Country: Number of subjects enrolled	Croatia: 7
Country: Number of subjects enrolled	Denmark: 12
Country: Number of subjects enrolled	Australia: 51
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Germany: 104
Country: Number of subjects enrolled	Japan: 21
Worldwide total number of subjects	1369
EEA total number of subjects	551

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)	1065
From 65 to 84 years	304
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study contains a screening period, followed by randomization and an intensive insulin optimization period (0-12 weeks) when insulin is adjusted weekly, and a maintenance adjustment period (12-26 weeks).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	LY2605541 + Insulin Lispro

Arm description:

Participants were randomized to receive LY2605541 plus Insulin Lispro. Participant-specific dose of LY2605541 was administered subcutaneously (SC) once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial (pre-meal) and supplemental doses for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	LY2605541
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant-specific dose of LY2605541 was administered subcutaneously (SC) once daily at bedtime for 26 weeks.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	Humalog
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant-specific dose of Insulin Lispro was administered SC for preprandial (pre-meal) and supplemental doses for 26 weeks.

Arm title	Insulin Glargine + Insulin Lispro
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Arm description:

Participants were randomized to receive Insulin Glargine plus Insulin Lispro. Participant-specific dose of Insulin Glargine was administered SC once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial and supplemental doses for 26 weeks.

Arm type	Active comparator
Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant-specific dose of Insulin Glargine was administered SC once daily at bedtime for 26 weeks.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	Humalog
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participant-specific dose of Insulin Lispro was administered SC for preprandial and supplemental doses for 26 weeks.

Number of subjects in period 1	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro
Started	691	678
Received at least 1 dose of study drug	691	677
Completed	620	618
Not completed	71	60
Adverse event, serious fatal	4	1
Consent withdrawn by subject	28	28
Physician decision	8	15
Adverse event, non-fatal	12	9
Sponsor Decision	1	-
Lost to follow-up	10	5
Protocol deviation	8	2

Baseline characteristics

Reporting groups

Reporting group title	LY2605541 + Insulin Lispro
Reporting group description:	
Participants were randomized to receive LY2605541 plus Insulin Lispro. Participant-specific dose of LY2605541 was administered subcutaneously (SC) once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial (pre-meal) and supplemental doses for 26 weeks.	
Reporting group title	Insulin Glargine + Insulin Lispro
Reporting group description:	
Participants were randomized to receive Insulin Glargine plus Insulin Lispro. Participant-specific dose of Insulin Glargine was administered SC once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial and supplemental doses for 26 weeks.	

Reporting group values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro	Total
Number of subjects	691	678	1369
Age categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean	57.43	57.77	
standard deviation	± 9.21	± 9.17	-
Gender, Male/Female			
Units: Participants			
Female	315	274	589
Male	376	404	780
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	74	78	152
Not Hispanic or Latino	452	427	879
Unknown or Not Reported	165	173	338
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	2	2	4
Asian	25	30	55
Native Hawaiian or Other Pacific Islander	2	2	4
Black or African American	42	50	92
White	615	585	1200
More than one race	5	9	14
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
United States	276	270	546
Taiwan	7	8	15
Slovakia	25	17	42
Greece	12	11	23
Spain	30	35	65

Lithuania	4	2	6
Turkey	4	7	11
Austria	9	6	15
Russian Federation	19	20	39
Israel	20	20	40
United Kingdom	5	3	8
Italy	16	16	32
Czech Republic	23	22	45
Hungary	36	36	72
Mexico	13	12	25
Puerto Rico	20	26	46
Poland	20	20	40
Brazil	11	13	24
Romania	34	31	65
Croatia	5	2	7
Denmark	9	3	12
Australia	26	25	51
Netherlands	7	8	15
Germany	50	54	104
Japan	10	11	21

End points

End points reporting groups

Reporting group title	LY2605541 + Insulin Lispro
Reporting group description: Participants were randomized to receive LY2605541 plus Insulin Lispro. Participant-specific dose of LY2605541 was administered subcutaneously (SC) once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial (pre-meal) and supplemental doses for 26 weeks.	
Reporting group title	Insulin Glargine + Insulin Lispro
Reporting group description: Participants were randomized to receive Insulin Glargine plus Insulin Lispro. Participant-specific dose of Insulin Glargine was administered SC once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial and supplemental doses for 26 weeks.	

Primary: Change From Baseline in Hemoglobin A1c (HbA1c) at 26 Weeks

End point title	Change From Baseline in Hemoglobin A1c (HbA1c) at 26 Weeks
End point description: HbA1c is a test that measures a participant's average blood glucose level over a 2 to 3 month timeframe. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data at both baseline and post-baseline.	
End point type	Primary
End point timeframe: Baseline, 26 weeks	

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	672		
Units: percentage of HbA1c				
least squares mean (standard error)	-1.66 (± 0.04)	-1.45 (± 0.04)		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: 95% Confidence interval (CI) and Least Squares (LS) means were calculated using mixed model repeated measures (MMRM) adjusting for stratification factors (country, low-density lipoprotein cholesterol [LDL-C, less than (<) 100 milligrams per deciliter (mg/dL) and greater than or equal to (≥) 100 mg/dL], and number of insulin injections at baseline [1, 2, or ≥3]), visit, treatment, visit-by-treatment interaction, and baseline HbA1c.	
Comparison groups	LY2605541 + Insulin Lispro v Insulin Glargine + Insulin Lispro

Number of subjects included in analysis	1356
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	-0.11

Notes:

[1] - Non-inferiority margin was 0.4%.

Secondary: Total hypoglycemia rates (Adjusted for 30 days)

End point title	Total hypoglycemia rates (Adjusted for 30 days)
End point description:	
Hypoglycemic episodes are defined as events which are associated with reported signs and symptoms of hypoglycemia and/or documented blood glucose (BG) concentrations of less than or equal to (\leq) mg/dL (3.9 millimoles per liter [mmol/L]). Arithmetic mean rates of total hypoglycemia (per 30 days) are presented and were calculated from the mean of hypo rate of participants within each treatment. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.	
End point type	Secondary
End point timeframe:	
Baseline through 26 weeks	

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	689	676		
Units: episodes/participant/30 days				
arithmetic mean (standard deviation)	5.52 (\pm 5.27)	5.46 (\pm 5.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with total hypoglycemia episodes

End point title	Percentage of participants with total hypoglycemia episodes
End point description:	
Hypoglycemic episodes are defined as events which are associated with reported signs and symptoms of hypoglycemia and/or documented BG concentrations of \leq 70 mg/dL (3.9 mmol/L). The percentage of participants was calculated by dividing the number of participants with hypoglycemic episodes by the total number of participants analyzed, multiplied by 100. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.	
End point type	Secondary

End point timeframe:

Baseline through 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	689	676		
Units: percentage of participants				
number (not applicable)	95.2	96.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Nocturnal hypoglycemia rates (Adjusted for 30 days)

End point title	Nocturnal hypoglycemia rates (Adjusted for 30 days)
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End point description:

Hypoglycemic episodes are defined as events which are associated with reported signs and symptoms of hypoglycemia and/or a documented BG concentration of ≤ 70 mg/dL (3.9 mmol/L). A nocturnal hypoglycemic event occurred between bedtime and waking and between the time points of 10:00 PM and 10:00 AM. Arithmetic mean rates of nocturnal hypoglycemia (per 30 days) are presented and were calculated from the mean of hypo rate of participants within each treatment. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

Baseline through 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	689	676		
Units: events/participant/30 days				
arithmetic mean (standard deviation)	0.49 (\pm 0.85)	0.9 (\pm 1.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with nocturnal hypoglycemia episodes

End point title	Percentage of participants with nocturnal hypoglycemia episodes
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End point description:

Hypoglycemic episodes are defined as an event which is associated with reported signs and symptoms of hypoglycemia and/or a BG concentration of ≤ 70 mg/dL (3.9 mmol/L). A nocturnal hypoglycemic event occurred between bedtime and waking and between the time points of 10:00 PM and 10:00 AM. The percentage of participants was calculated by dividing the number of participants with nocturnal hypoglycemic episodes by the total number of participants analyzed, multiplied by 100. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

Baseline through 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	689	676		
Units: percentage of participants				
number (not applicable)	59.5	74		

Statistical analyses

No statistical analyses for this end point

Secondary: Body Weight Change From Baseline to 26 Weeks

End point title	Body Weight Change From Baseline to 26 Weeks
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End point description:

LS means were calculated using MMRM adjusting for stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and number of insulin injections at baseline [1, 2, or ≥ 3]), treatment, visit, treatment-by-visit interaction, and baseline body weight as fixed effects, and participant as a random effect. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable body weight data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

Baseline, 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	682	671		
Units: kilograms (kg)				
least squares mean (standard error)	1.25 (± 0.16)	2.21 (± 0.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Self-Monitored Blood Glucose (SMBG) 9-point profiles at 26 weeks

End point title	Self-Monitored Blood Glucose (SMBG) 9-point profiles at 26 weeks
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End point description:

9-point SMBG profiles were obtained over 2 nonconsecutive days within the week prior to Weeks 0, 4, 12, and 26. SMBG measurements were taken at 9 time points: pre-morning meal, 2 hours post-morning meal, pre-midday meal, 2 hours post-midday meal, pre-evening meal, 2 hours post-evening meal, bedtime, at approximately 0300 hours, and the subsequent morning prior to the morning meal. LS means were calculated using MMRM adjusting for stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and number of insulin injections at baseline [1, 2, or ≥ 3]), visit, treatment, visit-by-treatment interaction, and baseline BG values. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable SMBG data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	639	619		
Units: mg/dL				
least squares mean (standard error)				
Pre-morning meal (n=639, 619)	137.31 (\pm 1.63)	133.81 (\pm 1.66)		
2 hours post-morning meal (n=545, 538)	162.77 (\pm 2.59)	156.41 (\pm 2.64)		
Pre-midday meal (n=606, 584)	130.02 (\pm 1.97)	133.63 (\pm 2.02)		
2 hours post-midday meal (n=548, 550)	145.55 (\pm 2.67)	156.17 (\pm 2.72)		
Pre-evening meal (n=611, 595)	142.65 (\pm 2.09)	149.19 (\pm 2.14)		
2 hours post-evening meal (n=552, 536)	156.56 (\pm 2.72)	166.59 (\pm 2.85)		
Bedtime (n=587, 557)	160.15 (\pm 2.6)	163.62 (\pm 2.7)		
0300 hours (n=516, 487)	143.9 (\pm 2.54)	140.19 (\pm 2.59)		
Pre-morning meal next day (n=605, 588)	135.09 (\pm 1.77)	132.07 (\pm 1.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HbA1c $< 7.0\%$ and $\leq 6.5\%$ at 26 weeks

End point title	Percentage of participants with HbA1c $< 7.0\%$ and $\leq 6.5\%$ at 26
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End point description:

The percentage of participants was calculated by dividing the number of participants reaching target HbA1c by the total number of participants analyzed, multiplied by 100. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data. Missing endpoints were imputed with the last observation carried forward (LOCF) method, using only post-baseline data.

End point type

Secondary

End point timeframe:

up to 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	672		
Units: percentage of participants				
number (not applicable)				
HbA1c $\leq 6.5\%$	44.4	32.6		
HbA1c $< 7.0\%$	63.3	53.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HbA1c $< 7.0\%$ without nocturnal hypoglycemia at 26 weeks

End point title

Percentage of participants with HbA1c $< 7.0\%$ without nocturnal hypoglycemia at 26 weeks

End point description:

Hypoglycemic episodes are defined as an event which is associated with reported signs and symptoms of hypoglycemia and/or a documented blood glucose concentration of ≤ 70 mg/dL (3.9 mmol/L). A nocturnal hypoglycemic event occurred between bedtime and waking and between the time points of 10:00 PM and 10:00 AM. The percentage of participants was calculated by dividing the number of participants with HbA1c $< 7.0\%$ without nocturnal hypoglycemia by the total number of participants analyzed, multiplied by 100. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data. Missing endpoints were imputed with the LOCF method, using only post-baseline data.

End point type

Secondary

End point timeframe:

up to 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	672		
Units: percentage of participants				
number (not applicable)	23.7	12.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Basal, bolus, and total insulin dose by weight at 26 weeks

End point title	Basal, bolus, and total insulin dose by weight at 26 weeks
End point description:	
Basal insulin dose, short-acting bolus insulin dose (each meal and overall), and total insulin dose were calculated based on the dose during the last 7 days prior to the post-treatment visit or last 3 days prior to the randomization visit. LS means were calculated using a constrained Longitudinal Data Analysis (cLDA) model adjusting for indicator variables of each treatment group at each post-baseline visit and stratification variables (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, baseline LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and baseline number of insulin injections [1, 2, or ≥ 3]). Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable insulin dose data.	
End point type	Secondary
End point timeframe:	
26 weeks	

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	613		
Units: units/kg/day				
least squares mean (standard error)				
Basal Insulin (n=612, 606)	0.68 (± 0.01)	0.6 (± 0.01)		
Bolus Insulin (n=591, 591)	0.61 (± 0.02)	0.63 (± 0.02)		
Total Insulin (n=615, 613)	1.27 (± 0.02)	1.21 (± 0.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting serum glucose (FSG) from laboratory at 26 weeks

End point title	Fasting serum glucose (FSG) from laboratory at 26 weeks
End point description:	
LS means were calculated using MMRM adjusting for stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and number of insulin injections at baseline	

[1, 2, or ≥3]), treatment, visit, treatment-by-visit interaction, and baseline FSG. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable FSG data at both baseline and post-baseline.

End point type	Secondary
End point timeframe:	
26 weeks	

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	683	672		
Units: mg/dL				
least squares mean (standard error)	125.33 (± 1.93)	132.02 (± 1.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Fasting blood glucose (FBG) (by SMBG) Intra-participant Variability at 26 Weeks

End point title	Fasting blood glucose (FBG) (by SMBG) Intra-participant Variability at 26 Weeks
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End point description:

FBG was measured by self-monitored blood glucose (SMBG). Between-day glucose variability is measured by the standard deviation of FBG. LS means were calculated using MMRM adjusting for the stratification factors (baseline HbA1c [≤8.5% and >8.5%], country, baseline LDL-C [<100 mg/dL and ≥100 mg/dL], and number of insulin injections at baseline [1, 2, or ≥3]), treatment, visit, treatment-by-visit interaction, and baseline FBG variability. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable FBG data at both baseline and post-baseline.

End point type	Secondary
End point timeframe:	
26 weeks	

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	674	652		
Units: mg/dL				
least squares mean (standard error)	28.67 (± 0.79)	33.54 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: 0300-hour blood glucose to FBG excursion at 26 weeks

End point title	0300-hour blood glucose to FBG excursion at 26 weeks
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End point description:

Results of a 0300-hour to pre-morning meal (FBG) excursion are presented (only SMBG profiles with both 0300 hours and the next day pre-morning measurements are included for the calculation of such excursion). LS means were calculated using MMRM adjusting for stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, baseline LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and number of insulin injections at baseline [1, 2, or ≥ 3]), treatment, visit, treatment-by-visit interaction, and baseline excursion. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable SMBG data at baseline and post-baseline.

End point type	Secondary
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End point timeframe:

26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	470	450		
Units: mg/dL				
least squares mean (standard error)	-11.95 (\pm 2.34)	-15.16 (\pm 2.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: HbA1c at 26 weeks

End point title	HbA1c at 26 weeks
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End point description:

HbA1c is a test that measures a participant's average blood glucose level over the past 2 to 3 months. LS means were calculated using MMRM adjusting for stratification factors (country, LDL-C [< 100 mg/dL and ≥ 100 mg/dL], and number of insulin injections at baseline [1, 2, or ≥ 3]), treatment, visit, treatment, visit-by-treatment interaction, and baseline HbA1c. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable HbA1c data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	672		
Units: percentage of HbA1c				
least squares mean (standard error)	6.76 (± 0.04)	6.97 (± 0.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Lipid profile at 26 weeks

End point title	Lipid profile at 26 weeks
End point description: Concentrations of cholesterol, high-density lipoprotein cholesterol (HDL-C), LDL-C, and triglycerides are summarized. LS means were calculated using MMRM adjusting for stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, LDL-C [< 100 mg/dL and ≥ 100 mg/dL], except for the LDL-C outcome variable], number of insulin injections at baseline [1, 2, or ≥ 3]), visit, treatment, visit-by-treatment interaction, and baseline value of corresponding lipid outcome variable. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable lipid data at both baseline and post-baseline.	
End point type	Secondary
End point timeframe: 26 weeks	

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	684	674		
Units: mg/dL				
least squares mean (standard error)				
Cholesterol (n=613, 609)	177.17 (± 1.13)	174.79 (± 1.14)		
HDL-C (n=611, 603)	46.44 (± 0.27)	47.71 (± 0.27)		
LDL-C (n=609, 603)	97.87 (± 0.99)	98.89 (± 0.99)		
Triglycerides (n=614, 609)	168.79 (± 2.85)	141.78 (± 2.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with change in anti-LY2605541 antibodies from baseline to 26 weeks

End point title	Number of participants with change in anti-LY2605541 antibodies from baseline to 26 weeks
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End point description:

The number of participants with a treatment-emergent anti-LY2605541 antibody response (TEAR) is summarized. TEAR is defined as change from baseline to post-baseline in the anti-LY2605541 antibody level either from undetectable to detectable, or from detectable to the value with at least 130% relative increase from baseline. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable anti-LY2605541 antibody data at baseline and post-baseline.

End point type	Secondary
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End point timeframe:

Baseline through 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	682	672		
Units: participants				
number (not applicable)	152	161		

Statistical analyses

No statistical analyses for this end point

Secondary: Insulin Treatment Satisfaction Questionnaire (ITSQ) at 26 weeks

End point title	Insulin Treatment Satisfaction Questionnaire (ITSQ) at 26 weeks
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End point description:

ITSQ is a validated instrument containing 22 items that assess treatment satisfaction for participants with diabetes and on insulin. The questionnaire measures satisfaction from the following 5 domains: Inconvenience of Regimen, Lifestyle Flexibility, Glycemic Control, Hypoglycemic Control, Insulin Delivery Device. Data presented are the transformed overall score on a scale of 0-100, where higher scores indicate better treatment satisfaction. LS means were calculated using an analysis of covariance (ANCOVA) model with treatment and stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, and baseline number of insulin injections [1, 2, or ≥ 3]) as fixed effects and baseline value of the ITSQ scores as a covariate. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable ITSQ data at both baseline and post-baseline. Missing endpoints were imputed with the LOCF method.

End point type	Secondary
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End point timeframe:

up to 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	631	637		
Units: units on a scale				
least squares mean (standard error)	77.01 (± 0.55)	77.29 (± 0.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Low Blood Sugar Survey (LBSS) at 26 weeks

End point title	Low Blood Sugar Survey (LBSS) at 26 weeks
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End point description:

LBSS (also referenced as Hypoglycemia Fear Survey – II [HFS-II]) is a 33-item questionnaire that measures 1) behaviors to avoid hypoglycemia and its negative consequences (15 items) and 2) worries about hypoglycemia and its negative consequences (18 items). Responses are made on a 5-point Likert scale where 0 = Never and 4 = Always. Total score is the sum of all items (range 0-132). Higher total scores reflect greater fear of hypoglycemia. LS means were calculated using MMRM including stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, baseline number of insulin injections [1, 2, or ≥ 3]), visit, treatment, visit-by-treatment interaction, and baseline LBSS score. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable LBSS data at both baseline and post-baseline.

End point type	Secondary
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End point timeframe:

26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	682	671		
Units: units on a scale				
least squares mean (standard error)	21.44 (± 0.56)	21.67 (± 0.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL-5D (EQ-5D) at 26 weeks

End point title	EuroQoL-5D (EQ-5D) at 26 weeks
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End point description:

The EQ-5D is a generic, multidimensional, health-related, quality-of-life instrument. The profile allows participants to rate their health state in 5 health domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression using a three level scale of 1-3 (no problem, some problems, and extreme problems). These combinations of attributes are converted into a weighted health-state Index Score according to the United States population-based algorithm. Scores range from -0.11 to 1.0, where a score of 1.0 indicates perfect health. LS means were calculated using ANCOVA adjusting for treatment, stratification factors (baseline HbA1c [$\leq 8.5\%$ and $> 8.5\%$], country, and baseline number of insulin injections [1, 2, or ≥ 3]), and baseline EQ-5D score. Analysis population included participants who were randomized, had at least 1 dose of study medication, and had evaluable EQ-5D data at both baseline and post-baseline. Missing endpoints were imputed with the LOCF method.

End point type	Secondary
End point timeframe:	
up to 26 weeks	

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	636	644		
Units: units on a scale				
least squares mean (standard error)	0.86 (± 0)	0.85 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rapid Assessment of Physical Activity (RAPA) at 26 weeks

End point title	Rapid Assessment of Physical Activity (RAPA) at 26 weeks
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End point description:

The RAPA questionnaire assesses the level and intensity of physical activity of adult participants (pts). It contains 2 subscales: RAPA 1 (Aerobic) and RAPA 2 (Strength and Flexibility). RAPA 1 contains 7 questions regarding the pts amount and intensity of physical activity, allowing each pts aerobic activity level to be categorized as sedentary, underactive, light activities, regular underactive, or active. RAPA 2 contains 2 questions regarding pts physical activities that increase strength and improve flexibility. Each pts strength and flexibility activity level is then categorized as neither, either or both strength and/or flexibility activity. Percentage of pts in each RAPA 1/2 category is presented and calculated by dividing the number of pts by the total number of pts analyzed, multiplied by 100. Analysis population included pts who were randomized, had at least 1 dose of study medication, evaluable RAPA data. Missing endpoints were imputed with LOCF method, using only post-baseline data.

End point type	Secondary
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End point timeframe:

up to 26 weeks

End point values	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	331	346		
Units: percentage of participants				
number (not applicable)				
RAPA 1, Sedentary (n=324, 339)	2.2	2.4		
RAPA 1, Underactive (n=324, 339)	4.6	6.2		
RAPA 1, Light activity (n=324, 339)	21.9	18		
RAPA 1, Regular underactive (n=324, 339)	32.7	27.1		
RAPA 1, Active (n=324, 339)	38.6	46.3		
RAPA 2, Neither strength/flexibility (n=331, 346)	58.3	53.8		

RAPA 2, Either strength/flexibility (n=331, 346)	28.1	30.6		
RAPA 2, Both strength/flexibility (n=331, 346)	13.6	15.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	LY2605541 + Insulin Lispro
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Reporting group description:

Includes participants that were randomized to receive LY2605541 plus Insulin Lispro. Participant-specific dose of LY2605541 was administered subcutaneously (SC) once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial (pre-meal) and supplemental doses for 26 weeks.

Reporting group title	Insulin Glargine + Insulin Lispro
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Reporting group description:

Includes participants that were randomized to receive Insulin Glargine plus Insulin Lispro. Participant-specific dose of Insulin Glargine was administered SC once daily at bedtime for 26 weeks. Participant-specific dose of Insulin Lispro was administered SC for preprandial and supplemental doses for 26 weeks.

Serious adverse events	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro	
Total subjects affected by serious adverse events			
subjects affected / exposed	79 / 691 (11.43%)	63 / 677 (9.31%)	
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			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
breast cancer			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

large intestine benign neoplasm alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ovarian cancer alternative dictionary used: MedDRA 16.0 subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostate cancer alternative dictionary used: MedDRA 16.0 subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostate cancer metastatic alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectal adenocarcinoma alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
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 alternative dictionary used: MedDRA 16.0 subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertensive crisis alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intermittent claudication			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
subclavian artery stenosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
venous insufficiency			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
coronary arterial stent insertion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
knee arthroplasty			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (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			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
death			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
medical device complication			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
anaphylactic shock			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
drug hypersensitivity			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypersensitivity			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
sarcoidosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
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			
postmenopausal haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
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			
dyspnoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea exertional			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pleural effusion			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary congestion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary oedema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory distress			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
adjustment disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
depression			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
panic attack			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
catheterisation cardiac			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
acetabulum fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bone contusion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
contusion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
coronary artery restenosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
excoriation			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
fall			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
femur fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
head injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
injury			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
lower limb fracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
medication error			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

road traffic accident alternative dictionary used: MedDRA 16.0 subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
skull fractured base alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
subdural haematoma alternative dictionary used: MedDRA 16.0 subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
tibia fracture alternative dictionary used: MedDRA 16.0 subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
traumatic haematoma alternative dictionary used: MedDRA 16.0 subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper limb fracture alternative dictionary used: MedDRA 16.0 subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders acute myocardial infarction alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina pectoris			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
angina unstable			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac arrest			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
cardiac failure			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac failure acute			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

cardio-respiratory arrest alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
coronary artery disease alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 691 (0.43%)	2 / 677 (0.30%)		
occurrences causally related to treatment / all	0 / 4	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
coronary artery stenosis alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	3 / 691 (0.43%)	0 / 677 (0.00%)		
occurrences causally related to treatment / all	1 / 3	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
hypertensive heart disease alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
myocardial infarction alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)		
occurrences causally related to treatment / all	0 / 2	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
nodal arrhythmia alternative dictionary used: MedDRA 16.0				
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
ventricular tachycardia alternative dictionary used: MedDRA 16.0				

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
carotid artery stenosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebrovascular accident			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic hyperosmolar coma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoglycaemic unconsciousness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic stroke			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
transient ischaemic attack			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	3 / 691 (0.43%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
inner ear disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vertigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
cataract			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
panophthalmitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
anal fistula			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bezoar			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
crohn's disease			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematochezia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
inguinal hernia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

large intestine polyp			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophagitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal obstruction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
umbilical hernia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
cholecystitis acute			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholelithiasis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
drug-induced liver injury alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic cirrhosis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders blister alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders calculus ureteric alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nephrolithiasis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure acute alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure chronic			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract obstruction			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
hyperparathyroidism primary			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
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			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bursitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
exostosis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intervertebral disc protrusion alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
mobility decreased alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
musculoskeletal chest pain alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myalgia alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteoarthritis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rhabdomyolysis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

rotator cuff syndrome alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal column stenosis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal disorder alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (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			
appendicitis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchitis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 691 (0.43%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic foot infection alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
enterococcal infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
incision site infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
infected skin ulcer			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
infectious mononucleosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteomyelitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 691 (0.43%)	3 / 677 (0.44%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	

rotavirus infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 691 (0.00%) 0 / 0 0 / 0	1 / 677 (0.15%) 0 / 1 0 / 0	
subcutaneous abscess alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 691 (0.14%) 0 / 1 0 / 0	0 / 677 (0.00%) 0 / 0 0 / 0	
viral infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 691 (0.14%) 0 / 1 0 / 0	0 / 677 (0.00%) 0 / 0 0 / 0	
wound infection alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 691 (0.14%) 0 / 1 0 / 0	0 / 677 (0.00%) 0 / 0 0 / 0	
Metabolism and nutrition disorders fluid overload alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 691 (0.14%) 0 / 1 0 / 0	0 / 677 (0.00%) 0 / 0 0 / 0	
hypoglycaemia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	18 / 691 (2.60%) 9 / 21 0 / 0	12 / 677 (1.77%) 7 / 15 0 / 0	

Non-serious adverse events	LY2605541 + Insulin Lispro	Insulin Glargine + Insulin Lispro	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	408 / 691 (59.04%)	406 / 677 (59.97%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
basal cell carcinoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences (all)	2	0	
benign neoplasm			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
benign neoplasm of thyroid gland			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
chronic lymphocytic leukaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
melanocytic naevus			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
skin papilloma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
thyroid adenoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
thyroid neoplasm			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Vascular disorders			
arterial disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
arteriosclerosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
arteritis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
deep vein thrombosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
essential hypertension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
flushing			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
haematoma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	3 / 677 (0.44%)	
occurrences (all)	1	3	
hot flush			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
hypertension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	14 / 691 (2.03%)	12 / 677 (1.77%)	
occurrences (all)	16	12	
hypertensive crisis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences (all)	2	0	
hypotension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences (all)	2	0	
orthostatic hypotension			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences (all)	2	0	
peripheral ischaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
varicose vein			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences (all)	0	2	
Surgical and medical procedures			
abscess drainage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
anal fistula excision			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
angioplasty		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
appendicectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
atherectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
bone graft		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
cardiac ablation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
carpal tunnel decompression		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	2	0
cataract operation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	1 / 677 (0.15%)
occurrences (all)	4	1
cholecystectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2

coronary angioplasty			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
coronary arterial stent insertion			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)	
occurrences (all)	2	1	
coronary artery bypass			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
craniotomy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
dental implantation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
dental operation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
dental prosthesis placement			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
endodontic procedure			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
explorative laparotomy			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
eye laser surgery		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
fracture treatment		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
gastrostomy tube insertion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
hip arthroplasty		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
inguinal hernia repair		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
intervertebral disc operation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
joint manipulation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
knee arthroplasty		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1

knee operation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
laser therapy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
leg amputation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
ligament operation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
malignant tumour excision			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
medical device implantation			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
medical device removal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
myringotomy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
nail operation			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
nasal polypectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
oophorectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
open reduction of fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
osteosynthesis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
ovarian operation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
photocoagulation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
polypectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
radical prostatectomy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

renal stone removal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
retinal laser coagulation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
rotator cuff repair		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
sebaceous cyst excision		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
shoulder operation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
skin graft		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
skin neoplasm excision		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
spinal fusion surgery		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
stent placement		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
surgery		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
tendon operation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
tendon sheath incision		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
toe amputation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
tooth extraction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	4 / 677 (0.59%)
occurrences (all)	3	4
umbilical hernia repair		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
ureteral stent insertion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
ureteric calculus removal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1

uterine dilation and curettage alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
varicose vein operation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 2	0 / 677 (0.00%) 0	
wart excision alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
wound treatment alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
Pregnancy, puerperium and perinatal conditions pregnancy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
General disorders and administration site conditions asthenia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	7 / 677 (1.03%) 7	
chest discomfort alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	2 / 677 (0.30%) 2	
chest pain alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	5 / 691 (0.72%) 5	5 / 677 (0.74%) 6	

chills		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
face oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
fat tissue increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
fatigue		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	6 / 691 (0.87%)	16 / 677 (2.36%)
occurrences (all)	8	16
feeling abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
feeling jittery		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
gait disturbance		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
generalised oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
hunger		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
inflammation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
influenza like illness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	0 / 677 (0.00%)
occurrences (all)	5	0
injection site bruising		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	4 / 677 (0.59%)
occurrences (all)	2	4
injection site discolouration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
injection site erythema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	0 / 677 (0.00%)
occurrences (all)	4	0
injection site hypersensitivity		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
injection site hypertrophy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
injection site induration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

injection site inflammation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
injection site oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
injection site pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
injection site pruritus		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
injection site swelling		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
irritability		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
malaise		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
nodule		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
non-cardiac chest pain		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)
occurrences (all)	2	2
oedema peripheral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	11 / 691 (1.59%)	26 / 677 (3.84%)
occurrences (all)	11	31
pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
polyp		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
pyrexia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	8 / 691 (1.16%)	7 / 677 (1.03%)
occurrences (all)	8	7
secretion discharge		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
temperature intolerance		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
thirst		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

ulcer alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	3 / 677 (0.44%) 3	
Immune system disorders			
allergy to arthropod sting alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
contrast media allergy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
drug hypersensitivity alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	1 / 677 (0.15%) 1	
food allergy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	1 / 677 (0.15%) 1	
hypersensitivity alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	1 / 677 (0.15%) 1	
multiple allergies alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
reaction to food additive alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
seasonal allergy alternative dictionary used: MedDRA 16.0			

subjects affected / exposed occurrences (all)	4 / 691 (0.58%) 5	3 / 677 (0.44%) 3	
Social circumstances menopause alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
Reproductive system and breast disorders benign prostatic hyperplasia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	2 / 677 (0.30%) 2	
breast mass alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	0 / 677 (0.00%) 0	
erectile dysfunction alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	1 / 677 (0.15%) 1	
fibrocystic breast disease alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
menstruation irregular alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
metrorrhagia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
posthitis alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
prostatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)	
occurrences (all)	1	2	
testicular hypertrophy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
uterine pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
vaginal disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
allergic bronchitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
asthma			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 691 (0.72%)	2 / 677 (0.30%)	
occurrences (all)	5	2	
atelectasis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
cough		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	11 / 691 (1.59%)	12 / 677 (1.77%)
occurrences (all)	11	12
dysphonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
dyspnoea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	7 / 677 (1.03%)
occurrences (all)	5	7
dyspnoea exertional		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	3 / 677 (0.44%)
occurrences (all)	0	3
epistaxis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	0 / 677 (0.00%)
occurrences (all)	5	0
increased upper airway secretion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
interstitial lung disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
laryngeal inflammation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	3	0

nasal congestion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	3 / 677 (0.44%)
occurrences (all)	4	3
oropharyngeal pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	6 / 691 (0.87%)	6 / 677 (0.89%)
occurrences (all)	6	7
pharyngeal inflammation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
pleural effusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
pneumothorax		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
productive cough		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
pulmonary mass		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
pulmonary oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
respiratory disorder		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	1 / 677 (0.15%) 1	
respiratory tract congestion alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	2 / 677 (0.30%) 2	
rhinitis allergic alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 3	2 / 677 (0.30%) 2	
rhinorrhoea alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	1 / 677 (0.15%) 1	
sinus congestion alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	6 / 691 (0.87%) 6	5 / 677 (0.74%) 5	
sleep apnoea syndrome alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	1 / 677 (0.15%) 1	
vocal cord inflammation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
Psychiatric disorders anxiety alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 691 (0.43%) 3	4 / 677 (0.59%) 4	
bipolar disorder alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
confusional state		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
depressed mood		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
depression		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	7 / 677 (1.03%)
occurrences (all)	4	7
depressive symptom		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
homicidal ideation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
insomnia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	4 / 677 (0.59%)
occurrences (all)	4	4
libido decreased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
nervousness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

sleep disorder alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
stress alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
suicidal ideation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
Hepatobiliary disorders cholelithiasis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	1 / 677 (0.15%) 1	
hepatic function abnormal alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
hepatic steatosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 691 (0.43%) 3	0 / 677 (0.00%) 0	
hepatomegaly alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
hyperbilirubinaemia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
Investigations			

alanine aminotransferase increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	11 / 691 (1.59%)	2 / 677 (0.30%)
occurrences (all)	12	3
angiogram		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
arteriogram coronary		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
arthroscopy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
aspartate aminotransferase increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 691 (1.01%)	1 / 677 (0.15%)
occurrences (all)	7	1
biopsy skin		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
blood bilirubin increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)
occurrences (all)	2	2
blood creatine phosphokinase abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
blood creatine phosphokinase increased		

alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	9 / 677 (1.33%)
occurrences (all)	2	9
blood creatinine increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
blood iron decreased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
blood lactate dehydrogenase increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
blood pressure increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	2	0
blood triglycerides increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	2 / 677 (0.30%)
occurrences (all)	4	2
blood uric acid abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
blood uric acid increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
body temperature increased		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
bronchoscopy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
catheterisation cardiac		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
colonoscopy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
cystoscopy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
ecg signs of myocardial ischaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
electrocardiogram abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
electrocardiogram change		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
endoscopy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1

eosinophil count increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
haematocrit decreased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
haematocrit increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
haemoglobin decreased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	1 / 677 (0.15%) 1	
haemoglobin increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
heart rate increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	1 / 677 (0.15%) 1	
heart rate irregular alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
hepatic enzyme abnormal alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
hepatic enzyme increased alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	3 / 691 (0.43%)	2 / 677 (0.30%)
occurrences (all)	4	2
liver function test abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)
occurrences (all)	2	2
platelet count increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
protein urine present		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
qrs axis abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
red blood cell count increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
renal function test abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
transaminases increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
ureteroscopy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

urine calcium alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
weight decreased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 691 (0.43%) 3	0 / 677 (0.00%) 0	
weight increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	5 / 691 (0.72%) 5	8 / 677 (1.18%) 8	
white blood cell count increased alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
Injury, poisoning and procedural complications anaemia postoperative alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
ankle fracture alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
arthropod bite alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 3	3 / 677 (0.44%) 3	
arthropod sting alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	1 / 677 (0.15%) 1	
brain contusion alternative dictionary used:			

MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
burns second degree		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
burns third degree		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
cartilage injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
chest injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
concussion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
contusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	8 / 677 (1.18%)
occurrences (all)	6	9
drug administration error		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	3
epicondylitis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
excoriation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	0 / 677 (0.00%)
occurrences (all)	3	0
fall		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)
occurrences (all)	2	2
femur fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
foot fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	1 / 677 (0.15%)
occurrences (all)	5	1
foreign body		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
foreign body in eye		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
hand fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
head injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1

humerus fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
joint injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
keratorhexis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
laceration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)
occurrences (all)	2	2
ligament sprain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	4 / 677 (0.59%)
occurrences (all)	1	4
limb injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	2	0
lip injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
lower limb fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
medication error		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
muscle rupture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
muscle strain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	7 / 677 (1.03%)
occurrences (all)	3	9
optic nerve injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
patella fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
procedural pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	2 / 677 (0.30%)
occurrences (all)	4	3
radius fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
rib fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
road traffic accident		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

spinal column injury		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
spinal compression fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
sunburn		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
tendon rupture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
thermal burn		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
tibia fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
upper limb fracture		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
wound		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	1 / 677 (0.15%)
occurrences (all)	5	1
wrist fracture		
alternative dictionary used: MedDRA 16.0		

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 691 (0.14%)</p> <p>1</p>	<p>1 / 677 (0.15%)</p> <p>1</p>	
<p>wrong technique in drug usage process</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 691 (0.14%)</p> <p>1</p>	<p>0 / 677 (0.00%)</p> <p>0</p>	
<p>Congenital, familial and genetic disorders</p> <p>gilbert's syndrome</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 691 (0.00%)</p> <p>0</p> <p>talipes</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 691 (0.00%)</p> <p>0</p> <p>type v hyperlipidaemia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 691 (0.00%)</p> <p>0</p>	<p>1 / 677 (0.15%)</p> <p>1</p> <p>1 / 677 (0.15%)</p> <p>1</p> <p>1 / 677 (0.15%)</p> <p>1</p>	
<p>Cardiac disorders</p> <p>angina unstable</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 691 (0.00%)</p> <p>0</p> <p>aortic valve sclerosis</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 691 (0.14%)</p> <p>1</p> <p>arrhythmia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 691 (0.00%)</p> <p>0</p> <p>atrial fibrillation</p> <p>alternative dictionary used: MedDRA 16.0</p>	<p>1 / 677 (0.15%)</p> <p>1</p> <p>0 / 677 (0.00%)</p> <p>0</p> <p>1 / 677 (0.15%)</p> <p>1</p>	

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
atrial flutter		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
atrioventricular block		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
bradycardia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
bundle branch block left		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
bundle branch block right		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
cardiac discomfort		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
cardiac disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
cardiac failure congestive		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	1 / 677 (0.15%)
occurrences (all)	4	1

cardiomegaly		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
coronary artery disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
left ventricular failure		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
left ventricular hypertrophy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
myocardial infarction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
palpitations		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	1 / 677 (0.15%)
occurrences (all)	4	1
pericardial effusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	2
sinus arrest		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
sinus tachycardia		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	3 / 677 (0.44%) 3	
supraventricular extrasystoles alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
tachycardia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	3 / 677 (0.44%) 3	
Nervous system disorders			
ageusia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
amnesia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
burning sensation alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
carotid artery stenosis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
carpal tunnel syndrome alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	10 / 691 (1.45%) 11	1 / 677 (0.15%) 1	
cerebral microangiopathy alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
decreased vibratory sense		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
diabetic neuropathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	5 / 677 (0.74%)
occurrences (all)	5	5
dizziness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 691 (1.30%)	10 / 677 (1.48%)
occurrences (all)	11	10
dysgeusia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
dyskinesia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
guillain-barre syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
headache		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	12 / 691 (1.74%)	19 / 677 (2.81%)
occurrences (all)	12	20
hypoesthesia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 691 (1.01%)	7 / 677 (1.03%)
occurrences (all)	8	9

iird nerve paralysis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
intercostal neuralgia alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
lethargy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 691 (0.43%) 3	0 / 677 (0.00%) 0	
memory impairment alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
migraine alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	5 / 691 (0.72%) 5	3 / 677 (0.44%) 3	
monomelic amyotrophy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
mononeuropathy alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
nerve compression alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
neuropathy peripheral alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	3 / 691 (0.43%)	5 / 677 (0.74%)
occurrences (all)	3	5
paraesthesia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	3 / 677 (0.44%)
occurrences (all)	7	3
parkinson's disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
petit mal epilepsy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
polyneuropathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
presyncope		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
radiculitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
radiculopathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
restless legs syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

sciatica		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	6 / 677 (0.89%)
occurrences (all)	1	6
sinus headache		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
somnolence		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
syncope		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
tension headache		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
transient ischaemic attack		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
tremor		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	0 / 677 (0.00%)
occurrences (all)	3	0
trigeminal neuralgia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
viith nerve paralysis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
vertebrobasilar insufficiency			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)	
occurrences (all)	2	2	
bone marrow oedema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
eosinophilia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
increased tendency to bruise			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
iron deficiency anaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
leukocytosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
lymphadenitis			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
lymphadenopathy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
lymphadenopathy mediastinal			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
microcytic anaemia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
thrombocytopenia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			
deafness neurosensory			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
ear pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	4 / 677 (0.59%)	
occurrences (all)	2	4	
otorrhoea			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
tinnitus			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	4 / 677 (0.59%)	
occurrences (all)	0	4	
vertigo			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	3 / 677 (0.44%)	
occurrences (all)	2	3	
Eye disorders			
blepharospasm			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	2	
cataract			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 691 (0.43%)	3 / 677 (0.44%)	
occurrences (all)	3	4	
cataract nuclear			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
conjunctival haemorrhage			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
conjunctivitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)	
occurrences (all)	2	2	
conjunctivitis allergic			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)	
occurrences (all)	1	2	
diabetic keratopathy			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
diabetic retinopathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 691 (1.01%)	5 / 677 (0.74%)
occurrences (all)	8	5
dry eye		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
eye haemorrhage		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
eye inflammation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
eye irritation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
eye pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
glaucoma		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
iritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1

keratitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
lacrimation increased		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
macular degeneration		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
macular hole		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
macular oedema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	3 / 677 (0.44%)
occurrences (all)	2	3
ocular discomfort		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
ocular hypertension		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
optic ischaemic neuropathy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
presbyopia		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
retinopathy			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)	
occurrences (all)	1	2	
retinopathy hypertensive			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
trichiasis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
vision blurred			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)	
occurrences (all)	1	2	
visual impairment			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)	
occurrences (all)	2	0	
vitreous opacities			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 691 (0.58%)	1 / 677 (0.15%)	
occurrences (all)	4	1	
abdominal distension			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	3 / 691 (0.43%)	2 / 677 (0.30%)
occurrences (all)	3	3
abdominal hernia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
abdominal pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 691 (1.01%)	4 / 677 (0.59%)
occurrences (all)	7	4
abdominal pain lower		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
abdominal pain upper		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	3 / 677 (0.44%)
occurrences (all)	4	3
abdominal tenderness		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
acquired oesophageal web		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
anal fissure		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
anal fistula		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	2

constipation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 691 (1.30%)	6 / 677 (0.89%)
occurrences (all)	9	6
dental caries		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
diarrhoea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	24 / 691 (3.47%)	19 / 677 (2.81%)
occurrences (all)	27	22
diverticulum		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
dry mouth		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	2
duodenal ulcer		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
dyspepsia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	2 / 677 (0.30%)
occurrences (all)	5	2
dysphagia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
enterocolitis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
eosinophilic oesophagitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
eructation		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
faeces pale		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
flatulence		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
food poisoning		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
gastric ulcer		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
gastritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	3 / 677 (0.44%)
occurrences (all)	1	3
gastrointestinal hypermotility		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

gastroesophageal reflux disease		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	7 / 691 (1.01%)	4 / 677 (0.59%)
occurrences (all)	7	4
gingival pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
haematochezia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	2	0
haemorrhoids		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
hiatus hernia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
infrequent bowel movements		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
intestinal obstruction		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
irritable bowel syndrome		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
large intestine polyp		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	3 / 677 (0.44%)
occurrences (all)	1	5
melaena		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
nausea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	16 / 691 (2.32%)	9 / 677 (1.33%)
occurrences (all)	16	10
oesophageal stenosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
oral pruritus		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	2	0
rectal haemorrhage		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
toothache		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	0 / 677 (0.00%)
occurrences (all)	4	0
varices oesophageal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
vomiting		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	11 / 691 (1.59%)	10 / 677 (1.48%)
occurrences (all)	11	13

Skin and subcutaneous tissue disorders			
acanthosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
acne			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
actinic keratosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
alopecia			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences (all)	0	2	
angioedema			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
blister			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	2	1	
dermal cyst			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)	
occurrences (all)	2	1	
dermatitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	2	
dermatitis allergic			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
dermatitis contact		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
diabetic foot		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
dry skin		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
eczema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	2 / 677 (0.30%)
occurrences (all)	4	2
erythema		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	3
hair growth abnormal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
hidradenitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
hirsutism		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0

hyperhidrosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	6 / 677 (0.89%)
occurrences (all)	3	6
hyperkeratosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
ingrowing nail		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
ingrown hair		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
lipodystrophy acquired		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
lipohypertrophy		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 691 (1.30%)	0 / 677 (0.00%)
occurrences (all)	11	0
neurodermatitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
night sweats		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
pruritus		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	7 / 691 (1.01%)	1 / 677 (0.15%)
occurrences (all)	7	1
rash		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	9 / 691 (1.30%)	7 / 677 (1.03%)
occurrences (all)	9	8
rash erythematous		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
rash generalised		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
rash maculo-papular		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
rosacea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
skin fissures		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	2
skin lesion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
skin mass		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0

<p>skin swelling</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 691 (0.00%)</p> <p>0</p>	<p>1 / 677 (0.15%)</p> <p>1</p>	
<p>skin ulcer</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 691 (0.58%)</p> <p>5</p>	<p>3 / 677 (0.44%)</p> <p>4</p>	
<p>swelling face</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 691 (0.00%)</p> <p>0</p>	<p>1 / 677 (0.15%)</p> <p>1</p>	
<p>urticaria</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 691 (0.00%)</p> <p>0</p>	<p>1 / 677 (0.15%)</p> <p>2</p>	
<p>Renal and urinary disorders</p> <p>bladder disorder</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dysuria</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>haematuria</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>leukocyturia</p> <p>alternative dictionary used: MedDRA 16.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>microalbuminuria</p> <p>alternative dictionary used: MedDRA 16.0</p>	<p>0 / 691 (0.00%)</p> <p>0</p> <p>1 / 691 (0.14%)</p> <p>1</p> <p>1 / 691 (0.14%)</p> <p>1</p> <p>0 / 691 (0.00%)</p> <p>0</p>	<p>1 / 677 (0.15%)</p> <p>1</p> <p>1 / 677 (0.15%)</p> <p>1</p> <p>1 / 677 (0.15%)</p> <p>1</p>	

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
nephrolithiasis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	3 / 677 (0.44%)
occurrences (all)	0	3
nocturia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
pollakiuria		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
proteinuria		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
renal colic		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
renal cyst		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
renal failure acute		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
renal failure chronic		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0

urinary incontinence alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
urinary retention alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
urine odour abnormal alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
Endocrine disorders autoimmune thyroiditis alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	1 / 677 (0.15%) 1	
goitre alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	2 / 691 (0.29%) 2	1 / 677 (0.15%) 1	
hypogonadism alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	0 / 691 (0.00%) 0	2 / 677 (0.30%) 2	
hypothyroidism alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	3 / 691 (0.43%) 3	0 / 677 (0.00%) 0	
thyroid cyst alternative dictionary used: MedDRA 16.0 subjects affected / exposed occurrences (all)	1 / 691 (0.14%) 1	0 / 677 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

arthralgia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	15 / 691 (2.17%)	15 / 677 (2.22%)
occurrences (all)	17	20
arthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	4 / 677 (0.59%)
occurrences (all)	2	4
back pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	22 / 691 (3.18%)	23 / 677 (3.40%)
occurrences (all)	25	25
bursitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	4 / 677 (0.59%)
occurrences (all)	3	4
chondromalacia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
coccydynia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
exostosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	2
fibromyalgia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
flank pain		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	3 / 691 (0.43%)	3 / 677 (0.44%)
occurrences (all)	3	4
gouty arthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
groin pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
intervertebral disc disorder		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
intervertebral disc protrusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	2	2
joint effusion		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
joint hyperextension		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
joint swelling		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)
occurrences (all)	2	2
lumbar spinal stenosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1

medial tibial stress syndrome			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	2	
muscle contracture			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
muscle disorder			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
muscle spasms			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 691 (0.72%)	5 / 677 (0.74%)	
occurrences (all)	5	5	
muscle tightness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
muscle twitching			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
musculoskeletal pain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	6 / 691 (0.87%)	8 / 677 (1.18%)	
occurrences (all)	7	10	
musculoskeletal stiffness			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
myalgia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	4 / 691 (0.58%)	5 / 677 (0.74%)
occurrences (all)	4	5
myositis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
neck pain		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	5 / 677 (0.74%)
occurrences (all)	3	5
nodal osteoarthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
osteoarthritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	5 / 677 (0.74%)
occurrences (all)	3	5
osteochondrosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
osteoporosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
pain in extremity		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	10 / 691 (1.45%)	14 / 677 (2.07%)
occurrences (all)	10	14
pain in jaw		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	3 / 677 (0.44%)
occurrences (all)	2	5

plantar fasciitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	4 / 691 (0.58%)	1 / 677 (0.15%)	
occurrences (all)	4	2	
rheumatoid arthritis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
rotator cuff syndrome			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
sacroiliitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
spondylitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
systemic lupus erythematosus			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
tendonitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	5 / 677 (0.74%)	
occurrences (all)	2	5	
tenosynovitis stenosans			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)	
occurrences (all)	1	1	
trigger finger			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	1 / 691 (0.14%)	3 / 677 (0.44%)	
occurrences (all)	1	3	
vertebral foraminal stenosis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Infections and infestations			
abscess jaw			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
abscess limb			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
acute sinusitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)	
occurrences (all)	2	1	
acute tonsillitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)	
occurrences (all)	0	2	
anal fistula infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
arthritis infective			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
atypical pneumonia			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
bacterial infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
body tinea		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
bronchitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	20 / 691 (2.89%)	20 / 677 (2.95%)
occurrences (all)	21	22
bronchopneumonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
burn infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
candidiasis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
carbuncle		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	2	0
cellulitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	6 / 691 (0.87%)	2 / 677 (0.30%)
occurrences (all)	6	2

chronic hepatitis b		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
chronic sinusitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
conjunctivitis viral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
cystitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	3 / 677 (0.44%)
occurrences (all)	5	3
dengue fever		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
diverticulitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
dysentery		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
ear infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	6 / 691 (0.87%)	3 / 677 (0.44%)
occurrences (all)	6	3
erysipelas		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	2 / 677 (0.30%)
occurrences (all)	1	4
escherichia infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
eye infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
fungus infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	2 / 677 (0.30%)
occurrences (all)	3	2
fungus skin infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
furuncle		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
gastroenteritis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	8 / 691 (1.16%)	16 / 677 (2.36%)
occurrences (all)	9	16
gastroenteritis viral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	12 / 691 (1.74%)	6 / 677 (0.89%)
occurrences (all)	12	6
gastrointestinal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	3 / 677 (0.44%)
occurrences (all)	1	3

herpes ophthalmic		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
herpes zoster		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	3 / 677 (0.44%)
occurrences (all)	5	3
infected bites		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
influenza		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	18 / 691 (2.60%)	16 / 677 (2.36%)
occurrences (all)	19	17
injection site infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
kidney infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
labyrinthitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
laryngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	2 / 677 (0.30%)
occurrences (all)	4	2
localised infection		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
lower respiratory tract infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
nail bed infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
nail infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
nasopharyngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	49 / 691 (7.09%)	63 / 677 (9.31%)
occurrences (all)	58	69
onychomycosis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	1 / 677 (0.15%)
occurrences (all)	3	1
oral candidiasis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
oral infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
otitis externa		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	3	1

otitis media		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	4 / 677 (0.59%)
occurrences (all)	0	4
otitis media acute		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
paronychia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
pharyngitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	7 / 677 (1.03%)
occurrences (all)	3	7
pharyngitis streptococcal		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
pharyngotonsillitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
pneumonia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	4 / 691 (0.58%)	4 / 677 (0.59%)
occurrences (all)	4	4
post procedural infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
pyelonephritis		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
pyoderma		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	2
rectal abscess		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
respiratory tract infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
respiratory tract infection viral		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
rhinitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	3 / 677 (0.44%)
occurrences (all)	0	3
rhinovirus infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
sinusitis		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	16 / 691 (2.32%)	12 / 677 (1.77%)
occurrences (all)	19	13
skin infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1

subcutaneous abscess		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
tonsillitis bacterial		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
tooth abscess		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	5 / 677 (0.74%)
occurrences (all)	3	5
tooth infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	2 / 677 (0.30%)
occurrences (all)	3	2
upper respiratory tract infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	29 / 691 (4.20%)	32 / 677 (4.73%)
occurrences (all)	33	39
urinary tract infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	18 / 691 (2.60%)	23 / 677 (3.40%)
occurrences (all)	19	26
vaginal infection		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	2 / 677 (0.30%)
occurrences (all)	0	2
vaginitis bacterial		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
viral infection		
alternative dictionary used: MedDRA 16.0		

subjects affected / exposed	4 / 691 (0.58%)	4 / 677 (0.59%)	
occurrences (all)	4	4	
viral pharyngitis			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
viral upper respiratory tract infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	5 / 691 (0.72%)	5 / 677 (0.74%)	
occurrences (all)	8	5	
vulvovaginal mycotic infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)	
occurrences (all)	1	0	
wound infection			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
abnormal loss of weight			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	0 / 691 (0.00%)	3 / 677 (0.44%)	
occurrences (all)	0	3	
abnormal weight gain			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	2 / 691 (0.29%)	6 / 677 (0.89%)	
occurrences (all)	2	8	
decreased appetite			
alternative dictionary used: MedDRA 16.0			
subjects affected / exposed	3 / 691 (0.43%)	0 / 677 (0.00%)	
occurrences (all)	4	0	
dehydration			
alternative dictionary used: MedDRA 16.0			

subjects affected / exposed	3 / 691 (0.43%)	1 / 677 (0.15%)
occurrences (all)	3	1
dyslipidaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
fluid retention		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	2 / 677 (0.30%)
occurrences (all)	2	2
gout		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	0 / 677 (0.00%)
occurrences (all)	6	0
hyperglycaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	3 / 677 (0.44%)
occurrences (all)	1	3
hyperkalaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
hyperlipidaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	2	0
hypernatraemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	0 / 691 (0.00%)	1 / 677 (0.15%)
occurrences (all)	0	1
hypertriglyceridaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1

hyperuricaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	5 / 691 (0.72%)	3 / 677 (0.44%)
occurrences (all)	5	3
hypokalaemia		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
increased appetite		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	0 / 677 (0.00%)
occurrences (all)	2	0
iron deficiency		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
obesity		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	2 / 691 (0.29%)	1 / 677 (0.15%)
occurrences (all)	2	1
vitamin b complex deficiency		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	1 / 677 (0.15%)
occurrences (all)	1	1
vitamin b12 deficiency		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	1 / 691 (0.14%)	0 / 677 (0.00%)
occurrences (all)	1	0
vitamin d deficiency		
alternative dictionary used: MedDRA 16.0		
subjects affected / exposed	3 / 691 (0.43%)	1 / 677 (0.15%)
occurrences (all)	3	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