



Clinical trial results:

A Randomized, Double-Blind, Placebo-Controlled Parallel Study with an Open-Label Extension to Assess the Impact of Testosterone Solution on Total Testosterone, Sex Drive and Energy in Hypogonadal Men

Summary

EudraCT number	2012-004866-16
Trial protocol	DE IT GB ES
Global end of trial date	30 April 2015

Results information

Result version number	v1 (current)
This version publication date	15 May 2016
First version publication date	15 May 2016

Trial information

Trial identification

Sponsor protocol code	I5E-MC-TSAT
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01816295
WHO universal trial number (UTN)	-

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	30 April 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate if testosterone solution can raise testosterone hormone levels into the normal range, and also improve levels of sexual arousal, interest and drive and/or energy level, in men with low testosterone and decreased sexual arousal, interest and drive and/or decreased energy. The study will last about 16 weeks, followed by an optional 24 week open label treatment phase to investigate the long term safety of testosterone solution.

Protection of trial subjects:

This study was conducted in accordance with 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	22 May 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 58
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Spain: 40
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Italy: 52
Country: Number of subjects enrolled	Korea, Republic of: 74
Country: Number of subjects enrolled	Puerto Rico: 7
Country: Number of subjects enrolled	United States: 432
Worldwide total number of subjects	715
EEA total number of subjects	120

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	572
From 65 to 84 years	141
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

No text entered.

Pre-assignment

Screening details:

Total testosterone level <300 nanograms per deciliter (ng/dL) [10.4 nanomole/liter (nmol/L)] obtained at each of the 2 screening visits, Screening Visit 1 and Screening Visit 2, performed at least 1 week apart

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Solution

Arm description:

Placebo solution applied topically to axillae once daily for 12 week double-blind treatment period. In optional open label extension (OLE) period, 60 milligram (mg) testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal solution
Routes of administration	Topical use

Dosage and administration details:

Placebo solution applied topically to axillae once daily for 12 week double-blind treatment period.

Arm title	Testosterone Solution
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Arm description:

Sixty mg testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 12 week double-blind treatment period. Optional OLE period starting at 60 mg/day with possible down/up titration (30 – 120 mg/day) for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Testosterone Solution
Investigational medicinal product code	
Other name	Axiron, Testosterone Solution 2%
Pharmaceutical forms	Transdermal solution
Routes of administration	Topical use

Dosage and administration details:

Testosterone Solution 60 milligram (mg) applied topically once daily with possible titration down to 30 milligram per day (mg/day) or up to 120 mg/day for 12 weeks and optional extension for 24 weeks.

Number of subjects in period 1	Placebo Solution	Testosterone Solution
Started	357	358
Received Study Drug	356	354
Completed	294	302
Not completed	63	56
Physician decision	2	2
Consent withdrawn by subject	22	20
Adverse event, non-fatal	11	8
Sponsor Decision	8	8
Lost to follow-up	3	5
Entry Criteria Not Met	-	2
Protocol deviation	17	11

Period 2

Period 2 title	Open Label Extension
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Solution

Arm description:

Placebo solution applied topically to axillae once daily for 12 week double-blind treatment period. In optional open label extension (OLE) period, 60 milligram (mg) testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal solution
Routes of administration	Topical use

Dosage and administration details:

Placebo solution applied topically to axillae once daily for 12 week double-blind treatment period.

Arm title	Testosterone Solution
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Arm description:

Sixty mg testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 12 week double-blind treatment period. Optional OLE period starting at 60 mg/day with possible down/up titration (30 – 120 mg/day) for 24 weeks.

Arm type	Experimental
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Investigational medicinal product name	Testosterone Solution
Investigational medicinal product code	
Other name	Axiron, Testosterone Solution 2%
Pharmaceutical forms	Transdermal solution
Routes of administration	Topical use

Dosage and administration details:

Testosterone Solution 60 milligram (mg) applied topically once daily with possible titration down to 30 milligram per day (mg/day) or up to 120 mg/day for 12 weeks and optional extension for 24 weeks.

Number of subjects in period 2^[1]	Placebo Solution	Testosterone Solution
Started	275	283
Completed	222	227
Not completed	53	56
Adverse event, serious fatal	1	-
Physician decision	3	1
Consent withdrawn by subject	10	10
Adverse event, non-fatal	17	15
Sponsor Decision	7	9
Lost to follow-up	5	5
Entry Criteria Not Met	3	5
Protocol deviation	4	4
Lack of efficacy	3	7

Notes:

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

Justification: Participants who completed the Double Blind Phase and still met eligibility criteria had the option to enroll in the Open Label Extension.

Baseline characteristics

Reporting groups

Reporting group title	Placebo Solution
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Reporting group description:

Placebo solution applied topically to axillae once daily for 12 week double-blind treatment period. In optional open label extension (OLE) period, 60 milligram (mg) testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 24 weeks.

Reporting group title	Testosterone Solution
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Reporting group description:

Sixty mg testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 12 week double-blind treatment period. Optional OLE period starting at 60 mg/day with possible down/up titration (30 – 120 mg/day) for 24 weeks.

Reporting group values	Placebo Solution	Testosterone Solution	Total
Number of subjects	357	358	715
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age Continuous Units: years			
arithmetic mean	55.9	54.7	
standard deviation	± 11.35	± 10.58	-
Gender, Male/Female Units: participants			
Female	0	0	0
Male	357	358	715
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	51	57	108
Not Hispanic or Latino	280	279	559
Unknown or Not Reported	26	22	48
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	1	4
Asian	38	45	83
Native Hawaiian or Other Pacific Islander	2	0	2
Black or African American	26	24	50
White	282	281	563
More than one race	6	7	13

Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
East Asia	34	40	74
Europe	63	57	120
South America	28	30	58
North America	232	231	463
Symptoms of Hypogonadism			
Units: Subjects			
Only Low Energy	49	47	96
Only Decreased Sexual Drive	39	40	79
Both Symptoms Present	269	271	540
Body Mass Index (BMI)			
BMI is an estimate of body fat based on body weight divided by height squared.			
Units: kilogram per square meter (kg/m ²)			
arithmetic mean	30.9	30.3	
standard deviation	± 4.21	± 4.06	-

End points

End points reporting groups

Reporting group title	Placebo Solution
Reporting group description: Placebo solution applied topically to axillae once daily for 12 week double-blind treatment period. In optional open label extension (OLE) period, 60 milligram (mg) testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 24 weeks.	
Reporting group title	Testosterone Solution
Reporting group description: Sixty mg testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 12 week double-blind treatment period. Optional OLE period starting at 60 mg/day with possible down/up titration (30 – 120 mg/day) for 24 weeks.	
Reporting group title	Placebo Solution
Reporting group description: Placebo solution applied topically to axillae once daily for 12 week double-blind treatment period. In optional open label extension (OLE) period, 60 milligram (mg) testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 24 weeks.	
Reporting group title	Testosterone Solution
Reporting group description: Sixty mg testosterone solution applied topically to axillae once daily with possible down/up titration (30 – 120 mg/day) for 12 week double-blind treatment period. Optional OLE period starting at 60 mg/day with possible down/up titration (30 – 120 mg/day) for 24 weeks.	

Primary: Number of Participants with Total Serum Testosterone Concentration within Normal Range at Week 12

End point title	Number of Participants with Total Serum Testosterone Concentration within Normal Range at Week 12
End point description: Normal range for total serum testosterone was defined as 300 to 1050 nanograms per deciliter (ng/dL) or 10.4-36.4 nmol/L.	
End point type	Primary
End point timeframe: Week 12	

End point values	Placebo Solution	Testosterone Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	287	297		
Units: participants				
number (not applicable)	43	217		

Statistical analyses

Statistical analysis title	Statistical Analysis for Primary Endpoint
Comparison groups	Placebo Solution v Testosterone Solution

Number of subjects included in analysis	584
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared
Confidence interval	
sides	2-sided

Secondary: Change from Baseline to Week 12 in Sexual Arousal, Interest, and Drive (SAID) Scale Scores

End point title	Change from Baseline to Week 12 in Sexual Arousal, Interest, and Drive (SAID) Scale Scores
End point description:	
<p>The SAID Scale is a self-administered instrument used to assess sexual arousal, interest, and sex drive in men with symptomatic hypogonadism. The SAID consists of 5 questions that were scored on a scale from 1 to 5, with "5" corresponding to greater levels of sexual arousal, interest, or drive. The SAID Scale total score was computed by summing the item scores and linearly transforming the sum to a 0 to 100 scale, with higher scores corresponding to greater sexual arousal, interest, and drive. Least squares (LS) mean change from baseline was calculated using an analysis of covariance (ANCOVA) with treatment group and the baseline value as covariates.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Placebo Solution	Testosterone Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	257	244		
Units: units on a scale				
least squares mean (standard error)	6.3 (± 0.99)	11.4 (± 1.02)		

Statistical analyses

Statistical analysis title	Statistical Analysis for SAID Scale Scores
Comparison groups	Placebo Solution v Testosterone Solution
Number of subjects included in analysis	501
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	5.1

Confidence interval	
level	Other: 99.5 %
sides	2-sided
lower limit	1.05
upper limit	9.07
Variability estimate	Standard error of the mean
Dispersion value	1.42

Secondary: Change from Baseline to Week 12 in Hypogonadism Energy Diary (HED) Scores

End point title	Change from Baseline to Week 12 in Hypogonadism Energy Diary (HED) Scores
End point description:	
<p>The HED is a self-administered instrument used to assess real-time energy levels in men with symptomatic hypogonadism. It consists of 2 questions that were scored on a scale from 0 to 10, with "10" corresponding to "Full of Energy" or "Not Tired at All" (The Tiredness scale was reverse-mapped, as it was collected with "10" corresponding to "Extreme Tiredness"). The questionnaire was completed 3 times daily (forming 6 unique items) for 7 consecutive days. Item scores were computed by averaging the values for each item across 7 days. If more than 2 days were missing for an item, the item score was missing. The total score was computed by summing the item scores and linearly transforming the sum to a 0 to 100 scale, with higher scores corresponding to greater energy. If any item score was missing, the total score was missing. LS mean change from baseline was calculated using ANCOVA with treatment group and the baseline value as covariates.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Week 12	

End point values	Placebo Solution	Testosterone Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	243	230		
Units: units on a scale				
least squares mean (standard error)	7.5 (± 0.87)	10.5 (± 0.89)		

Statistical analyses

Statistical analysis title	Statistical Analysis for HED Scores
Comparison groups	Placebo Solution v Testosterone Solution
Number of subjects included in analysis	473
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	2.9

Confidence interval	
level	Other: 99.5 %
sides	2-sided
lower limit	-0.59
upper limit	6.45
Variability estimate	Standard error of the mean
Dispersion value	1.25

Secondary: Number of Participants with Prostate Specific Antigen (PSA) >4 Nanogram/Milliliter (ng/mL)

End point title	Number of Participants with Prostate Specific Antigen (PSA) >4 Nanogram/Milliliter (ng/mL)
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End point description:

End point type	Secondary
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End point timeframe:

Double Blind Baseline, Week 12, Open Label Baseline, Week 36

End point values	Placebo Solution	Testosterone Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	350	347		
Units: participants				
number (not applicable)				
Double-Blind Baseline (n=350, 347)	1	0		
Week 12 (n=289, 299)	3	4		
Open Label Baseline (n=269, 278)	0	0		
Week 36 (n=219, 223)	4	4		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Total International Prostate Symptom Score (IPSS)

End point title	Change from Baseline in Total International Prostate Symptom Score (IPSS)
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End point description:

The IPSS is a self-administered instrument used to assess for the severity of lower urinary tract symptoms. The IPSS consists of 7 questions that were scored on a scale from 0 (none/no symptoms) to 5 (frequent symptoms), for a total score range of 0 to 35. Higher numerical scores from the IPSS questionnaire represent greater severity of symptoms. LS mean change from baseline was calculated using ANCOVA with treatment group and the baseline value as covariates.

End point type	Other pre-specified
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End point timeframe:

Baseline, Week 12, Week 36

End point values	Placebo Solution	Testosterone Solution		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	320	324		
Units: units on a scale				
least squares mean (standard error)				
Change from Baseline to Week 12	-0.7 (± 0.24)	-0.9 (± 0.24)		
Change from Baseline to Week 36 (n=247, 255)	-0.7 (± 0.28)	-0.7 (± 0.27)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for IPSS
Statistical analysis description: Change from Baseline to Week 36	
Comparison groups	Placebo Solution v Testosterone Solution
Number of subjects included in analysis	644
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.905
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	0.72
Variability estimate	Standard error of the mean
Dispersion value	0.39

Statistical analysis title	Statistical Analysis 2 for IPSS
Statistical analysis description: Change from Baseline to Week 12	
Comparison groups	Placebo Solution v Testosterone Solution
Number of subjects included in analysis	644
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.442
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.94
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.34

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Double-Blind and Open-Label Treatment Periods

Adverse event reporting additional description:

I5E-MC-TSAT

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Testosterone Solution
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Reporting group description: -

Reporting group title	Open-Label Testosterone
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Testosterone Solution	Open-Label Testosterone	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 354 (1.13%)	24 / 558 (4.30%)	8 / 356 (2.25%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
basal cell carcinoma			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
brain neoplasm			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholangiocarcinoma			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lentigo maligna alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung carcinoma cell type unspecified stage iv alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung neoplasm malignant alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
squamous cell carcinoma alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
venous thrombosis limb alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
non-cardiac chest pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
pneumothorax			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory failure			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
suicidal ideation			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicide attempt			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
brachial plexus injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chest injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
craniocerebral injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fall			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
foreign body			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haematuria traumatic alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
overdose alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rib fracture alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
scapula fracture alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper limb fracture alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders acute myocardial infarction alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
angina pectoris			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina unstable			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
cerebrovascular accident			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ischaemic stroke			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
seizure			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
cholelithiasis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
nephrolithiasis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intervertebral disc protrusion alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
musculoskeletal pain alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations bacterial disease carrier alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clostridium difficile colitis alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
endocarditis enterococcal alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
influenza alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
meningitis viral			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
septic embolus			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Testosterone Solution	Open-Label Testosterone	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	148 / 354 (41.81%)	252 / 558 (45.16%)	143 / 356 (40.17%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
acoustic neuroma			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
acrochordon			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	2 / 356 (0.56%)
occurrences (all)	0	0	2
infected neoplasm			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
melanocytic naevus			
alternative dictionary used:			

MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
neoplasm prostate			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
squamous cell carcinoma			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
Vascular disorders			
aortic aneurysm			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
flushing			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	2	1	0
hot flush			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
hypertension			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 354 (1.13%)	4 / 558 (0.72%)	4 / 356 (1.12%)
occurrences (all)	4	4	4
hypertensive crisis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
hypotension			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
peripheral vascular disorder			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
varicose vein			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
arthrodesis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
cataract operation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
corneal transplant			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
endodontic procedure			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
high frequency ablation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
inguinal hernia repair			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
knee arthroplasty			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
knee operation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
meniscus operation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	1	2	0
orthodontic procedure			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
posterior lens capsulotomy			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
rotator cuff repair			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
suture insertion			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
umbilical hernia repair			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0

vasectomy alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
vitrectomy alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
wisdom teeth removal alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
General disorders and administration site conditions application site acne alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
application site dryness alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
application site eczema alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
application site erythema alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	4 / 558 (0.72%) 4	3 / 356 (0.84%) 3
application site irritation alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	3 / 558 (0.54%) 3	0 / 356 (0.00%) 0
application site pain alternative dictionary used:			

MedDRA 18.0			
subjects affected / exposed	6 / 354 (1.69%)	2 / 558 (0.36%)	7 / 356 (1.97%)
occurrences (all)	6	2	7
application site pruritus			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
application site rash			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	4 / 558 (0.72%)	0 / 356 (0.00%)
occurrences (all)	0	4	0
application site reaction			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
application site warmth			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
asthenia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
axillary pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	2	0	0
chills			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
cyst			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
cyst rupture			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
effusion			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
fatigue			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 354 (1.13%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	4	2	0
haemorrhagic cyst			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
influenza like illness			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	2 / 356 (0.56%)
occurrences (all)	0	2	2
local swelling			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
non-cardiac chest pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	3 / 558 (0.54%)	1 / 356 (0.28%)
occurrences (all)	0	3	1
oedema			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0

oedema peripheral alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	3 / 354 (0.85%) 3	3 / 558 (0.54%) 3	0 / 356 (0.00%) 0
pain alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
peripheral swelling alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	1 / 356 (0.28%) 1
pyrexia alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
therapeutic response unexpected alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
Immune system disorders allergy to arthropod sting alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
drug hypersensitivity alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	1 / 356 (0.28%) 1
multiple allergies alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
Social circumstances			

alcohol use alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
sexual activity increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
substance use alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
Reproductive system and breast disorders balanoposthitis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
benign prostatic hyperplasia alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
breast mass alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
breast tenderness alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
erectile dysfunction alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	3 / 558 (0.54%) 3	0 / 356 (0.00%) 0
genital paraesthesia alternative dictionary used:			

MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
gynaecomastia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0
nipple disorder			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
nipple pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 354 (0.85%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	3	1	0
painful erection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
prostatomegaly			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	2 / 356 (0.56%)
occurrences (all)	1	1	2
pruritus genital			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
spermatic cord pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
testicular atrophy			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
testicular pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
testicular swelling			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 354 (1.13%)	7 / 558 (1.25%)	2 / 356 (0.56%)
occurrences (all)	4	7	2
dyspnoea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	3 / 558 (0.54%)	4 / 356 (1.12%)
occurrences (all)	1	3	4
epistaxis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
nasal congestion			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	1	3	0
oropharyngeal pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	4 / 558 (0.72%)	1 / 356 (0.28%)
occurrences (all)	1	5	1
respiratory tract congestion			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
rhinitis allergic			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	1	1	1
rhinorrhoea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
sinus congestion			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	1	2	0
sleep apnoea syndrome			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
upper-airway cough syndrome			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
aggression			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
agitation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
anger			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 354 (0.28%)	3 / 558 (0.54%)	1 / 356 (0.28%)
occurrences (all)	1	4	1
anxiety			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	6 / 558 (1.08%)	2 / 356 (0.56%)
occurrences (all)	2	6	2
bipolar disorder			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
depression			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	2	3	0
drug dependence			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
eating disorder			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
insomnia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 354 (0.85%)	3 / 558 (0.54%)	2 / 356 (0.56%)
occurrences (all)	3	3	2
irritability			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	1	2	0
libido decreased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0

libido increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
loss of libido			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
middle insomnia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
mood swings			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0
nervousness			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
personality disorder			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
premature ejaculation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
restlessness			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
sleep disorder			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	3 / 356 (0.84%) 3
Investigations			
alanine aminotransferase increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
aspartate aminotransferase increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
blood creatine phosphokinase abnormal alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
blood creatine phosphokinase increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
blood creatinine increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 558 (0.18%) 1	1 / 356 (0.28%) 1
blood follicle stimulating hormone increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
blood glucose decreased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
blood glucose increased alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	3 / 356 (0.84%)
occurrences (all)	0	1	3
blood insulin increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	2 / 356 (0.56%)
occurrences (all)	0	0	2
blood luteinising hormone increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
blood pressure increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	2 / 356 (0.56%)
occurrences (all)	0	2	2
blood testosterone increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	0	3	0
blood triglycerides increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
blood urea increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0
electrocardiogram p wave abnormal			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
electrocardiogram abnormal			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	2	0	0

electrocardiogram repolarisation abnormality alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
gamma-glutamyltransferase increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	2 / 356 (0.56%) 2
glycosylated haemoglobin increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	1 / 356 (0.28%) 1
haematocrit increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	9 / 354 (2.54%) 9	28 / 558 (5.02%) 28	2 / 356 (0.56%) 2
haemoglobin increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
hepatic enzyme increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
high density lipoprotein increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
liver function test abnormal alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
low density lipoprotein increased alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 354 (0.28%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	1	3	0
lymph node palpable			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
mean cell volume increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
prostatic specific antigen			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
prostatic specific antigen abnormal			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
prostatic specific antigen increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 354 (1.13%)	6 / 558 (1.08%)	2 / 356 (0.56%)
occurrences (all)	4	6	2
red blood cell count decreased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
red blood cell count increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0
weight decreased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	2	1	0

weight increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
Injury, poisoning and procedural complications			
ankle fracture alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	2 / 558 (0.36%) 2	0 / 356 (0.00%) 0
contusion alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
epicondylitis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	2 / 558 (0.36%) 2	0 / 356 (0.00%) 0
fall alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
fibula fracture alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
foot fracture alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
hand fracture alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
human bite alternative dictionary used:			

MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
joint dislocation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
joint injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
laceration			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	1	1	1
ligament rupture			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0
ligament sprain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
limb injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0
meniscus injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	2	2	1
muscle strain			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	0	3	0
procedural pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
rib fracture			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
skin abrasion			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	0	2	1
stress fracture			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
tendon injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
thermal burn			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
tibia fracture			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
tooth fracture			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1

wound alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
Cardiac disorders			
angina pectoris alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
atrial fibrillation alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
atrial flutter alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
atrioventricular block first degree alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
bradycardia alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
bundle branch block left alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
bundle branch block right alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
cardiac failure congestive alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
coronary artery disease			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
palpitations			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	2 / 356 (0.56%)
occurrences (all)	1	1	2
sinus bradycardia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	1	0	1
sinus tachycardia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
supraventricular extrasystoles			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
supraventricular tachycardia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
tachycardia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
ventricular extrasystoles			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1

Nervous system disorders			
burning sensation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	6 / 354 (1.69%)	0 / 558 (0.00%)	4 / 356 (1.12%)
occurrences (all)	7	0	5
carpal tunnel syndrome			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
cognitive disorder			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
diabetic neuropathy			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0
dizziness			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	4 / 558 (0.72%)	4 / 356 (1.12%)
occurrences (all)	0	4	4
dysgeusia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
epilepsy			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
headache			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 354 (0.85%)	7 / 558 (1.25%)	8 / 356 (2.25%)
occurrences (all)	3	7	8
hypoesthesia			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	2 / 354 (0.56%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	2	1	0
lumbar radiculopathy			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
memory impairment			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
mental impairment			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
neuropathy peripheral			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
paraesthesia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	2	1	0
paralysis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
presyncope			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
sciatica			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	1	1	0

sensory disturbance alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
sleep phase rhythm disturbance alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
syncope alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	3 / 558 (0.54%) 3	0 / 356 (0.00%) 0
trigeminal nerve disorder alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
writer's cramp alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
Blood and lymphatic system disorders anaemia alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 2	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
leukocytosis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
lymphadenopathy alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
polycythaemia alternative dictionary used: MedDRA 18.0			

subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
Ear and labyrinth disorders cerumen impaction alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
deafness neurosensory alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
middle ear effusion alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
tinnitus alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	2 / 558 (0.36%) 2	1 / 356 (0.28%) 1
vertigo alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	2 / 558 (0.36%) 2	0 / 356 (0.00%) 0
Eye disorders blepharospasm alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
dry eye alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
Gastrointestinal disorders abdominal discomfort alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
abdominal pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
abdominal pain lower			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
abdominal pain upper			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
chronic gastritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
constipation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
diarrhoea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	5 / 558 (0.90%)	4 / 356 (1.12%)
occurrences (all)	1	5	4
diverticulum			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
dyspepsia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	2	0	0

food poisoning			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
gastritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	1	1	1
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	2	1	1
gingival cyst			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
gingival pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
haemorrhoids			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	2	0	0
hypoesthesia oral			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
inguinal hernia			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
intestinal mass			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
irritable bowel syndrome			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
large intestine polyp			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	1	2	0
nausea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	2	1	1
oral pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
paraesthesia oral			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
rectal fissure			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
salivary duct obstruction			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1

tooth impacted alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 558 (0.18%) 2	0 / 356 (0.00%) 0
toothache alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	4 / 558 (0.72%) 4	0 / 356 (0.00%) 0
umbilical hernia alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
vomiting alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
Hepatobiliary disorders cholecystitis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
gallbladder polyp alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	0 / 558 (0.00%) 0	0 / 356 (0.00%) 0
hepatic cyst alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	0 / 356 (0.00%) 0
Skin and subcutaneous tissue disorders acne alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	10 / 558 (1.79%) 11	3 / 356 (0.84%) 3
actinic keratosis			

alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
dermatitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	2 / 558 (0.36%)	2 / 356 (0.56%)
occurrences (all)	2	3	2
dermatitis atopic			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
dermatitis contact			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	2	2	1
dry skin			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
eczema			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
erythema			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 354 (1.13%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	4	0	0
haemorrhage subcutaneous			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
hair growth abnormal			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
hyperhidrosis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	1	0	1
night sweats			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
pruritus			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 354 (0.85%)	3 / 558 (0.54%)	4 / 356 (1.12%)
occurrences (all)	3	3	4
rash			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 354 (1.13%)	2 / 558 (0.36%)	10 / 356 (2.81%)
occurrences (all)	4	2	11
rash erythematous			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
rash papular			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	3	0	1
skin burning sensation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	1	0	1
skin irritation			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 354 (1.13%)	0 / 558 (0.00%)	9 / 356 (2.53%)
occurrences (all)	5	0	9

<p>skin lesion</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 354 (0.00%)</p> <p>0</p>	<p>1 / 558 (0.18%)</p> <p>1</p>	<p>0 / 356 (0.00%)</p> <p>0</p>
<p>skin reaction</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 354 (0.28%)</p> <p>1</p>	<p>0 / 558 (0.00%)</p> <p>0</p>	<p>1 / 356 (0.28%)</p> <p>1</p>
<p>skin ulcer</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 354 (0.00%)</p> <p>0</p>	<p>0 / 558 (0.00%)</p> <p>0</p>	<p>1 / 356 (0.28%)</p> <p>1</p>
<p>urticaria</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 354 (0.28%)</p> <p>1</p>	<p>1 / 558 (0.18%)</p> <p>1</p>	<p>0 / 356 (0.00%)</p> <p>0</p>
<p>Renal and urinary disorders</p> <p>calculus urinary</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 354 (0.00%)</p> <p>0</p>	<p>0 / 558 (0.00%)</p> <p>0</p>	<p>1 / 356 (0.28%)</p> <p>1</p>
<p>diabetic nephropathy</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 354 (0.28%)</p> <p>1</p>	<p>0 / 558 (0.00%)</p> <p>0</p>	<p>0 / 356 (0.00%)</p> <p>0</p>
<p>dysuria</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 354 (0.28%)</p> <p>1</p>	<p>2 / 558 (0.36%)</p> <p>2</p>	<p>0 / 356 (0.00%)</p> <p>0</p>
<p>haematuria</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 354 (0.00%)</p> <p>0</p>	<p>2 / 558 (0.36%)</p> <p>2</p>	<p>0 / 356 (0.00%)</p> <p>0</p>
<p>lower urinary tract symptoms</p> <p>alternative dictionary used: MedDRA 18.0</p>			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
micturition disorder			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
nephrolithiasis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
nocturia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
pollakiuria			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	3 / 558 (0.54%)	1 / 356 (0.28%)
occurrences (all)	1	3	1
polyuria			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
urinary incontinence			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
urinary retention			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
urinary tract obstruction			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1

Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	8 / 354 (2.26%)	6 / 558 (1.08%)	4 / 356 (1.12%)
occurrences (all)	8	7	4
axillary mass			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	2	0	0
back pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	5 / 354 (1.41%)	16 / 558 (2.87%)	5 / 356 (1.40%)
occurrences (all)	5	16	5
exostosis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
foot deformity			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
intervertebral disc degeneration			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
joint swelling			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
lumbar spinal stenosis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
muscle spasms			
alternative dictionary used:			

MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	2	2	1
musculoskeletal chest pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
musculoskeletal pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	1	3	0
musculoskeletal stiffness			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
myalgia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	1	2	1
neck mass			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
neck pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	2	2	0
pain in extremity			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	2	2	1
plantar fasciitis			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
rotator cuff syndrome			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
spinal osteoarthritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
tendonitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
Infections and infestations			
abscess limb			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
acute sinusitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	1	1	1
application site pustules			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
arthritis infective			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
bronchitis			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 354 (0.28%)	7 / 558 (1.25%)	3 / 356 (0.84%)
occurrences (all)	1	7	4
candida infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
cellulitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	0	3	0
chest wall abscess			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
conjunctivitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
diarrhoea infectious			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
diverticulitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
ear infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	6 / 356 (1.69%)
occurrences (all)	0	0	6
erythema induratum			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0

folliculitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	1	2	1
fungus infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	0	2	1
fungus skin infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
furuncle			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	2 / 356 (0.56%)
occurrences (all)	0	0	2
gastroenteritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	3 / 356 (0.84%)
occurrences (all)	0	1	3
gastroenteritis viral			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	5 / 558 (0.90%)	0 / 356 (0.00%)
occurrences (all)	2	5	0
helicobacter infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
herpes zoster			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	1	1	1
hordeolum			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
influenza			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 354 (0.85%)	10 / 558 (1.79%)	3 / 356 (0.84%)
occurrences (all)	3	10	3
kidney infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
laryngitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
localised infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
nasal vestibulitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
nasopharyngitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	8 / 354 (2.26%)	19 / 558 (3.41%)	11 / 356 (3.09%)
occurrences (all)	8	21	11
oesophageal candidiasis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
onychomycosis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0

ophthalmic herpes zoster			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
oral candidiasis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
otitis media acute			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
paronychia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
periodontitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
pharyngitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	3 / 558 (0.54%)	1 / 356 (0.28%)
occurrences (all)	2	3	1
pharyngitis streptococcal			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
pneumonia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	4 / 558 (0.72%)	0 / 356 (0.00%)
occurrences (all)	0	4	0
pneumonia mycoplasmal			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
rhinitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	0 / 558 (0.00%)	1 / 356 (0.28%)
occurrences (all)	0	0	1
sinusitis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 354 (0.85%)	5 / 558 (0.90%)	2 / 356 (0.56%)
occurrences (all)	3	6	2
tinea cruris			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0
tinea pedis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	1 / 356 (0.28%)
occurrences (all)	0	1	1
tooth abscess			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	1	2	1
tooth infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
upper respiratory tract infection			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	8 / 354 (2.26%)	19 / 558 (3.41%)	6 / 356 (1.69%)
occurrences (all)	9	20	6
urethritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0

urinary tract infection alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	2 / 354 (0.56%) 2	3 / 558 (0.54%) 3	1 / 356 (0.28%) 1
viral upper respiratory tract infection alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	2 / 558 (0.36%) 2	1 / 356 (0.28%) 1
Metabolism and nutrition disorders			
decreased appetite alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
diabetes mellitus alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	1 / 558 (0.18%) 1	1 / 356 (0.28%) 1
dyslipidaemia alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	2 / 356 (0.56%) 2
fluid retention alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	1 / 558 (0.18%) 1	1 / 356 (0.28%) 1
glucose tolerance impaired alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 354 (0.00%) 0	0 / 558 (0.00%) 0	1 / 356 (0.28%) 1
gout alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 354 (0.28%) 1	4 / 558 (0.72%) 5	1 / 356 (0.28%) 2
hypercalcaemia alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 354 (0.28%)	0 / 558 (0.00%)	0 / 356 (0.00%)
occurrences (all)	1	0	0
hyperlipidaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 354 (0.85%)	0 / 558 (0.00%)	3 / 356 (0.84%)
occurrences (all)	3	0	3
hypertriglyceridaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 354 (0.56%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	2	2	1
hyperuricaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	1	2	0
hypoglycaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	1 / 356 (0.28%)
occurrences (all)	0	2	1
increased appetite			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	3 / 558 (0.54%)	0 / 356 (0.00%)
occurrences (all)	0	3	0
type 2 diabetes mellitus			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 354 (0.28%)	1 / 558 (0.18%)	2 / 356 (0.56%)
occurrences (all)	1	1	2
vitamin b complex deficiency			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	1 / 558 (0.18%)	0 / 356 (0.00%)
occurrences (all)	0	1	0
vitamin d deficiency			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 354 (0.00%)	2 / 558 (0.36%)	0 / 356 (0.00%)
occurrences (all)	0	2	0

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