Clinical trial results:
A Randomized Controlled Study to Compare the Safety and Efficacy of IPX203 with Immediate-Release Carbidopa-Levodopa in Parkinson's Disease Patients with Motor Fluctuations

Summary

EudraCT number	2018-002233-37
Trial protocol	CZ DE GB PL IT
Global end of trial date	15 June 2021

Results information

Result version number	v1 (current)
This version publication date	30 December 2022
First version publication date	30 December 2022

Trial information

Trial identification

Sponsor protocol code	IPX203-B16-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03670953
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Impax Laboratories, LLC
Sponsor organisation address	400 Crossing Boulevard , Bridgewater, United States, NJ 08807
Public contact	Pfitz Patrick, Impax Laboratories, LLC, +1 631-633-2104, pfitzpatrick@amneal.com
Scientific contact	Pfitz Patrick, Impax Laboratories, LLC, +1 631-633-2104, pfitzpatrick@amneal.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the safety and efficacy of IPX203 in comparison to immediate-release carbidopa-levodopa (IR CD-LD) in the treatment of CD-LD-experienced subjects with Parkinson’s disease who have motor fluctuations.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the International Conference on Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 November 2018
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	Poland: 78
Country: Number of subjects enrolled	Spain: 71
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Czechia: 45
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 48
Country: Number of subjects enrolled	Italy: 36
Country: Number of subjects enrolled	United States: 327
Worldwide total number of subjects	630
EEA total number of subjects	291

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	236
From 65 to 84 years	388
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 105 sites in the United States, Italy, Spain, France, the United Kingdom, the Czech Republic, Poland, and Germany. A total of 770 subjects were screened, of which 140 subjects were screen failures, and 630 subjects were enrolled in this study.

Pre-assignment

Screening details:

Study consisted of 4-week Screening period, 3 week open-label IR CD-LD dose adjustment period, 4 week open-label period for conversion to IPX203 and 13 week double-blind treatment period (DBP). Subjects were randomized in 1:1 ratio to receive either IPX203 (with matching IR CD-LD placebo) or IR CD-LD (with matching IPX203 placebo) in DBP.

Period 1

Period 1 title	IR CD-LD dose adjustment period(3 weeks)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	IR CD-LD Dose Adjustment

Arm description:

Subjects who were previously treated on a stable regimen with CD-LD for at least 4 weeks entered a 3-week, open-label IR CD-LD treatment period allowing for dose adjustment. During the IR CD-LD dose adjustment period, the initial dosing regimen of IR CD-LD was to be the same as the subject's stable pre-study regimen unless the subject was taking a single daily bedtime dose of controlled releases (CR) CD-LD. In such a case, the CR CD-LD dose was discontinued and substituted with a 1:1 milligram (mg)-equivalent dose of IR CD-LD.

Arm type	Active comparator
Investigational medicinal product name	IR CD-LD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received multiple doses of IR CD-LD oral tablets containing 25 mg CD and 100 mg LD.

Number of subjects in period 1	IR CD-LD Dose Adjustment
Started	630
Completed	589
Not completed	41
Consent withdrawn by subject	9
Adverse event, non-fatal	4
Unspecified	21
Lack of efficacy	1
Protocol deviation	6

Period 2

Period 2 title	Open-label Conversion Period to IPX203
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	IPX203 Dose Conversion period

Arm description:

Subjects who completed IR CD-LD dose adjustment period entered a 4-week open-label dose conversion period for conversion from IR CD-LD to IPX203. The initial dosing regimen of IPX203 was based on the most frequent dose of the subject's stable dosing regimen of IR CD-LD at the end of the dose adjustment period.

Arm type	Experimental
Investigational medicinal product name	IPX203 ER CD-LD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received multiple doses of IPX203 extended-release (ER) CD-LD oral capsules, containing 35 mg CD and 140 mg LD.

Number of subjects in period 2	IPX203 Dose Conversion period
Started	589
Completed	506
Not completed	83
Consent withdrawn by subject	32
Adverse event, non-fatal	35
Non-compliance with study drug	2
Unspecified	2
Lost to follow-up	1
Lack of efficacy	10
Protocol deviation	1

Period 3

Period 3 title	Double-Blind Maintenance Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	IPX203 Double-Blind Period

Arm description:

Subjects who successfully completed the IPX203 dose conversion period were randomized to receive multiple doses IPX203 35 mg CD and 140 mg LD ER oral capsules (with matching IR CD-LD placebo or multiple doses of IR CD-LD [with matching IPX203]) for up to 13 weeks of double-blind, double-dummy maintenance therapy with the stable dosing regimen established at the end of Week 7 for IPX203.

Arm type	Experimental
Investigational medicinal product name	IPX203
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received multiple doses of IPX203 CD-LD ER oral capsules, containing 35 mg CD and 140 mg LD.

Investigational medicinal product name	IR CD-LD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received IR CD-LD oral tablets.

Arm title	IR CD-LD Double-Blind Period

Arm description:

Subjects who successfully completed the IPX203 dose conversion period were randomized to receive multiple doses of IR CD-LD 25 mg CD and 100 mg LD oral tablets (with matching IPX203 placebo) for up to 13 weeks of double-blind, double-dummy maintenance therapy with the stable dosing regimen established at the end of Week 3 for IR CD-LD.

Arm type	Active comparator
Investigational medicinal product name	IR CD-LD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received multiple doses of IR CD-LD oral tablets containing 25 mg CD and 100 mg LD.

Investigational medicinal product name	Placebo matched to IPX203
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to IPX203 ER oral capsules.

Number of subjects in period 3	IPX203 Double-Blind Period	IR CD-LD Double-Blind Period
Started	256	250
Completed	222	227
Not completed	34	23
Consent withdrawn by subject	10	11
Adverse event, non-fatal	14	3
Non-compliance with study drug	1	-
Unspecified	1	-
Protocol deviation	3	1
Lack of efficacy	5	8

Baseline characteristics

Reporting groups	
Reporting group title	IR CD-LD Dose Adjustment

Reporting group description:

Subjects who were previously treated on a stable regimen with CD-LD for at least 4 weeks entered a 3-week, open-label IR CD-LD treatment period allowing for dose adjustment. During the IR CD-LD dose adjustment period, the initial dosing regimen of IR CD-LD was to be the same as the subject's stable pre-study regimen unless the subject was taking a single daily bedtime dose of controlled releases (CR) CD-LD. In such a case, the CR CD-LD dose was discontinued and substituted with a 1:1 milligram (mg)-equivalent dose of IR CD-LD.

Reporting group values	IR CD-LD Dose Adjustment	Total	
Number of subjects	630	630	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	66.5		
standard deviation	± 8.95	-	
Gender categorical Units: Subjects			
Female	234	234	
Male	396	396	
Race Units: Subjects			
American Indian/Alaska Native	3	3	
Asian	10	10	
Black/African American	6	6	
Native Hawaiian/Other Pacific Islander	0	0	
White	606	606	
Mixed	0	0	
Other	0	0	
Unknown or Not Reported	5	5	
Ethnicity Units: Subjects			
Not Hispanic or Latino	544	544	
Hispanic or Latino	77	77	
Not reported	9	9	
Unknown	0	0	

End points

End points reporting groups

Reporting group title	IR CD-LD Dose Adjustment

Reporting group description:

Subjects who were previously treated on a stable regimen with CD-LD for at least 4 weeks entered a 3-week, open-label IR CD-LD treatment period allowing for dose adjustment. During the IR CD-LD dose adjustment period, the initial dosing regimen of IR CD-LD was to be the same as the subject's stable pre-study regimen unless the subject was taking a single daily bedtime dose of controlled releases (CR) CD-LD. In such a case, the CR CD-LD dose was discontinued and substituted with a 1:1 milligram (mg)-equivalent dose of IR CD-LD.

Reporting group title	IPX203 Dose Conversion period

Reporting group description:

Subjects who completed IR CD-LD dose adjustment period entered a 4-week open-label dose conversion period for conversion from IR CD-LD to IPX203. The initial dosing regimen of IPX203 was based on the most frequent dose of the subject's stable dosing regimen of IR CD-LD at the end of the dose adjustment period.

Reporting group title	IPX203 Double-Blind Period

Reporting group description:

Subjects who successfully completed the IPX203 dose conversion period were randomized to receive multiple doses IPX203 35 mg CD and 140 mg LD ER oral capsules (with matching IR CD-LD placebo or multiple doses of IR CD-LD [with matching IPX203]) for up to 13 weeks of double-blind, double-dummy maintenance therapy with the stable dosing regimen established at the end of Week 7 for IPX203.

Reporting group title	IR CD-LD Double-Blind Period

Reporting group description:

Subjects who successfully completed the IPX203 dose conversion period were randomized to receive multiple doses of IR CD-LD 25 mg CD and 100 mg LD oral tablets (with matching IPX203 placebo) for up to 13 weeks of double-blind, double-dummy maintenance therapy with the stable dosing regimen established at the end of Week 3 for IR CD-LD.

Primary: Mean Change from Baseline in "Good on" Time in Hours per day, Averaged Over the Parkinson's disease (PD) Diary Days at the End of the Double-blind Treatment Period

End point title	Mean Change from Baseline in "Good on" Time in Hours per day, Averaged Over the Parkinson's disease (PD) Diary Days at the End of the Double-blind Treatment Period

End point description:

"Good on" time was derived from the 3-day PD Diaries and was defined as the sum of "On time without dyskinesia" and "On time with non-troublesome dyskinesia". The Modified Intent-to-treat (mITT) Analysis Set included all subjects who were randomized and treated and have a valid baseline PD Diary and at least one valid post-randomization PD Diary (using double-blind PD Diary baseline). Baseline was defined as data obtained from PD Diary collected over 3 days prior to Visit 4/Randomization (Week 7).

End point type	Primary

End point timeframe:

Baseline up to end of double-blind treatment period (Week 20)

End point values	IPX203 Double-Blind Period	IR CD-LD Double-Blind Period		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	246		
Units: hours per day				
least squares mean (standard error)	-0.50 (± 0.183)	-1.03 (± 0.183)		

Statistical analyses

Statistical analysis title	IPX203 vs IR CD-LD
Comparison groups	IR CD-LD Double-Blind Period v IPX203 Double-Blind Period
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0194 [1]
Method	MMRM model
Parameter estimate	Least square mean difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.97

Notes:

[1] - P-value was analyzed using a mixed model for repeated measures (MMRM) which included baseline "Good on" time as a covariate, treatment and visit (5, 6 or 7/ET) as fixed effects, pooled center as random effect and a treatment-by-visit interaction.

Secondary: Change from Baseline in "Off" Time in Hours per day, Averaged Over the PD Diary Days at the End of the Double-blind Treatment Period

End point title	Change from Baseline in "Off" Time in Hours per day, Averaged Over the PD Diary Days at the End of the Double-blind Treatment Period

End point description:

"Off" time was calculated by adding the number of half-hour intervals in which an "Off" was checked. The mITT analysis set included all subjects who were randomized and treated and have a valid baseline PD Diary and at least one valid post-randomization PD Diary (using double-blind PD Diary baseline). Baseline was defined as data obtained from PD Diary collected over 3 days prior to Visit 4/Randomization (Week 7).

End point type	Secondary

End point timeframe:

Baseline up to end of double-blind treatment period (Week 20)

End point values	IPX203 Double-Blind Period	IR CD-LD Double-Blind Period		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	249	246		
Units: hours per day				
least squares mean (standard error)	0.38 (± 0.172)	0.86 (± 0.171)		

Statistical analyses

Statistical analysis title	IPX203 vs IR CD-LD
Comparison groups	IPX203 Double-Blind Period v IR CD-LD Double-Blind Period
Number of subjects included in analysis	495
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0252 [2]
Method	MMRM model
Parameter estimate	LS Mean difference
Point estimate	-0.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.06

Notes:

[2] - P-value was analyzed using a MMRM which included baseline "Off" time as a covariate, treatment and visit (5, 6 or 7/ET) as fixed effects, pooled center as random effect and a treatment-by-visit interaction.

Secondary: Percentage of Subjects with Either "Much Improved" or "Very Much Improved" in Patient Global Impression of Change (PGI-C) Scores at the End of the Double-blind Treatment Period

End point title	Percentage of Subjects with Either "Much Improved" or "Very Much Improved" in Patient Global Impression of Change (PGI-C) Scores at the End of the Double-blind Treatment Period

End point description:

PGI-C was a single, subject-reported item reflecting the subject's impression of change in his/her disease status since the start of the study (that is, in relation to activity limitations, symptoms, emotions, and overall quality of life). Subjects rated their impression of change in disease status on a 7-point scale:1-very much improved; 2-much improved; 3-minimally improved; 4-no change; 5-minimally worse; 6-much worse; 7-very much worse where a higher score indicated worsening. Score ranges from 1 (Very Much Improved) to 7 (Very Much Worse). Lower scores indicate better health status. Percentage of subjects with either "Much Improved" or "Very Much Improved" PGI-C scores were reported. Intent-to-treat (ITT) Analysis Set included all subjects who were randomized and treated with any study drug and have a baseline and at least one post-baseline efficacy assessment (using double-blind baseline). "Number of subjects analyzed" signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

At the end of the double-blind treatment period (Week 20)

End point values	IPX203 Double-Blind Period	IR CD-LD Double-Blind Period		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	255	248		
Units: Percentage of subjects				
number (not applicable)				
Much Improved	26.7	18.5		
Very much Improved	3.1	0.4		

Statistical analyses

Statistical analysis title	IPX203 vs IR CD-LD
Comparison groups	IPX203 Double-Blind Period v IR CD-LD Double-Blind Period
Number of subjects included in analysis	503
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0015 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Percent difference
Point estimate	10.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.5
upper limit	18.3

Notes:

[3] - P-value from the Cochran-Mantel-Haenszel (CMH) test stratified by pooled center compared the percent of Much or Very Much Improved subjects between the treatment groups.

Secondary: Change from Baseline in the Movement Disorders Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III at the End of the Double-blind Treatment Period

End point title	Change from Baseline in the Movement Disorders Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III at the End of the Double-blind Treatment Period

End point description:

The MDS-UPDRS evaluates motor and non-motor symptoms in persons with Parkinson's and consists of 4 parts with various questions and evaluations. Part I (13 items; Score 0 to 52) examines non-motor experiences, Part II (13 items; Score 0 to 52) examines motor experiences, Part III (33 items; Score 0 to 132) examines the cardinal motor disabilities and Part IV (6 items; Score 0 to 24) examines motor complications. Each Part has 0 to 4 ratings, where 0 (no problems) to 4 (severe problems). Higher scores indicate a greater impact of Parkinson's disease symptoms (that is worse symptoms). The ITT analysis set included all subjects who were randomized and treated with any study drug and have a baseline and at least one post-baseline efficacy assessment (double-blind baseline). Baseline was defined as the last assessment obtained prior to the first dose of the randomized study drug.

End point type	Secondary

End point timeframe:

Baseline to the end of the double-blind treatment period (Week 20)

End point values	IPX203 Double-Blind Period	IR CD-LD Double-Blind Period		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	250		
Units: Score on a scale				
least squares mean (standard error)	0.8 (± 0.71)	0.8 (± 0.72)		

Statistical analyses

Statistical analysis title	IPX203 vs IR CD-LD
Comparison groups	IPX203 Double-Blind Period v IR CD-LD Double-Blind Period
Number of subjects included in analysis	506
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9587 [4]
Method	MMRM model
Parameter estimate	LS Mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.89

Notes:

[4] - P-value was analyzed using a MMRM which included baseline MDS as a covariate, treatment and visit (5, 6 or 7/ET) as fixed effects, pooled center as random effect and a treatment-by-visit interaction.

Secondary: Change from Baseline in the Sum of MDS-UPDRS Part II and III at the End of the Double-blind Treatment Period

End point title	Change from Baseline in the Sum of MDS-UPDRS Part II and III at the End of the Double-blind Treatment Period

End point description:

The MDS-UPDRS evaluates motor and non-motor symptoms in persons with Parkinson's and consists of 4 parts with various questions and evaluations. Part I (13 items; Score 0 to 52) examines non-motor experiences, Part II (13 items; Score 0 to 52) examines motor experiences, Part III (33 items; Score 0 to 132) examines the cardinal motor disabilities and Part IV (6 items; Score 0-24) examines motor complications. Each Part has 0 to 4 ratings, where 0 (no problems) to 4 (severe problems). Higher scores indicate a greater impact of Parkinson's disease symptoms (that is worse symptoms). Data was collected and analyzed as the sum of all answers in Parts II and III of the MDS-UPDRS questionnaire. ITT analysis set included all subjects who were randomized and treated with any study drug and have a baseline and at least one post-baseline efficacy assessment (double-blind baseline). Baseline was defined as the last assessment obtained prior to the first dose of the randomized study drug.

End point type	Secondary

End point timeframe:

Baseline to the end of the double-blind treatment period (Week 20)

End point values	IPX203 Double-Blind Period	IR CD-LD Double-Blind Period		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	250		
Units: Score on a scale				
least squares mean (standard error)	1.7 (± 0.87)	1.8 (± 0.87)		

Statistical analyses

Statistical analysis title	IPX203 vs IR CD-LD
Comparison groups	IPX203 Double-Blind Period v IR CD-LD Double-Blind Period
Number of subjects included in analysis	506
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9668 [5]
Method	MMRM model
Parameter estimate	LS Mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	1.11

Notes:

[5] - P-value was analyzed using a MMRM which included baseline MDS as a covariate, treatment and visit (5, 6 or 7/ET) as fixed effects, pooled center as random effect and a treatment-by-visit interaction.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to end of the double-blind treatment period (Week 20)

Adverse event reporting additional description:

The Safety Analysis Set included all subjects who were treated with any study drug (IPX203 or IR CD-LD).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	IR CD-LD Dose Adjustment Period

Reporting group description:

Subjects who were previously treated on a stable regimen with CD-LD for at least 4 weeks entered a 3-week, open-label IR CD-LD treatment period allowing for dose adjustment. During the IR CD-LD dose adjustment period, the initial dosing regimen of IR CD-LD was to be the same as the subject's stable pre-study regimen unless the subject was taking a single daily bedtime dose of CR CD-LD. In such a case, the CR CD-LD dose was discontinued and substituted with a 1:1 mg-equivalent dose of IR CD-LD.

Reporting group title	IPX203 Conversion Period

Reporting group description:

Subjects who completed IR CD-LD dose adjustment period entered a 4-week open-label dose conversion period for conversion from IR CD-LD to IPX203. The initial dosing regimen of IPX203 was based on the most frequent dose of the subject's stable dosing regimen of IR CD-LD at the end of the dose adjustment period.

Reporting group title	IPX203 Double-Blind Period

Reporting group description:

Subjects who successfully completed the IPX203 dose conversion period were randomized to receive multiple doses of IPX203 35 mg CD and 140 mg LD ER oral capsules (with matching IR CD-LD placebo or multiple doses of IR CD-LD [with matching IPX203]) for up to 13 weeks of double-blind, double-dummy maintenance therapy with the stable dosing regimen established at the end of Week 7 for IPX203.

Reporting group title	IR CD-LD Double-Blind Period

Reporting group description:

Subjects who successfully completed the IPX203 dose conversion period were randomized to receive multiple doses of IR CD-LD 25 mg CD and 100 mg LD oral tablets (with matching IPX203 placebo) for up to 13 weeks of double-blind, double-dummy maintenance therapy with the stable dosing regimen established at the end of Week 3 for IR CD-LD.

Serious adverse events	IR CD-LD Dose Adjustment Period	IPX203 Conversion Period	IPX203 Double-Blind Period
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 630 (1.11%)	12 / 589 (2.04%)	8 / 256 (3.13%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			

subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Surgical and medical procedures			
Inguinal hernia repair			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Fatigue			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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			
Hallucinations, mixed			

subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Ejection fraction decreased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Hip fracture			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Radiation neuropathy			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Skin laceration			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Subdural haematoma			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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			
Atrioventricular block complete			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bradycardia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Dyskinesia			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Epilepsy			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
On and off phenomenon			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Syncope			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (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
Vertebral artery aneurysm			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Gastrointestinal disorders			
Duodenitis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Inguinal hernia			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Nephrolithiasis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Urinary retention			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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

Urinary tract obstruction			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Epididymitis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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
Influenza			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Pneumonia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Pyelonephritis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sepsis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Urinary tract infection			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (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
Hyponatraemia			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (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

Serious adverse events	IR CD-LD Double-Blind Period		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 250 (1.60%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Inguinal hernia repair			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Asthenia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Benign prostatic hyperplasia				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Hallucinations, mixed				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Ejection fraction decreased				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				

Contusion				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiation neuropathy				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin laceration				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrioventricular block complete				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				

Cognitive disorder			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyskinesia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
On and off phenomenon			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertebral artery aneurysm			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Anaemia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Duodenitis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract obstruction				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				

subjects affected / exposed	1 / 250 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Cystitis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epididymitis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	1 / 250 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	IR CD-LD Dose Adjustment Period	IPX203 Conversion Period	IPX203 Double-Blind Period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	118 / 630 (18.73%)	229 / 589 (38.88%)	108 / 256 (42.19%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Extranodal marginal zone B-cell lymphoma (MALT type)			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Flushing			

subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Hypertension			
subjects affected / exposed	7 / 630 (1.11%)	4 / 589 (0.68%)	2 / 256 (0.78%)
occurrences (all)	7	4	2
Hypertensive crisis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Hypertensive urgency			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	0 / 630 (0.00%)	3 / 589 (0.51%)	1 / 256 (0.39%)
occurrences (all)	0	3	1
Labile hypertension			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Orthostatic hypotension			
subjects affected / exposed	5 / 630 (0.79%)	8 / 589 (1.36%)	2 / 256 (0.78%)
occurrences (all)	5	8	2
Peripheral venous disease			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Thrombosis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Varicophlebitis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	2 / 256 (0.78%)
occurrences (all)	0	0	2
General disorders and administration site conditions			

Balance disorder			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Feeling abnormal			
subjects affected / exposed	0 / 630 (0.00%)	3 / 589 (0.51%)	3 / 256 (1.17%)
occurrences (all)	0	3	3
Gait disturbance			
subjects affected / exposed	2 / 630 (0.32%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	2	0	1
Hernia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Mass			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	2 / 630 (0.32%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	3 / 256 (1.17%)
occurrences (all)	0	0	3
Pain			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0

Pyrexia			
subjects affected / exposed	2 / 630 (0.32%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	2	2	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Erectile dysfunction			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Prostatitis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Vaginal prolapse			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	2 / 256 (0.78%)
occurrences (all)	0	1	2
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 630 (0.16%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	1	2	0
Cough			
subjects affected / exposed	3 / 630 (0.48%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	3	1	1
Dry throat			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	3 / 256 (1.17%)
occurrences (all)	1	1	3

Oropharyngeal pain			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Pulmonary mass			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Sinus congestion			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 630 (0.16%)	5 / 589 (0.85%)	0 / 256 (0.00%)
occurrences (all)	1	5	0
Affect lability			
subjects affected / exposed	0 / 630 (0.00%)	3 / 589 (0.51%)	0 / 256 (0.00%)
occurrences (all)	0	3	0
Agitation			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	1 / 630 (0.16%)	9 / 589 (1.53%)	7 / 256 (2.73%)
occurrences (all)	1	9	7
Apathy			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Behaviour disorder			

subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Binge eating			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Bruxism			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Confusional state			
subjects affected / exposed	1 / 630 (0.16%)	4 / 589 (0.68%)	1 / 256 (0.39%)
occurrences (all)	1	4	1
Depressed mood			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 630 (0.00%)	7 / 589 (1.19%)	4 / 256 (1.56%)
occurrences (all)	0	7	4
Fear			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Hallucination			
subjects affected / exposed	1 / 630 (0.16%)	6 / 589 (1.02%)	2 / 256 (0.78%)
occurrences (all)	1	6	2
Hallucination, auditory			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Hallucination, visual			
subjects affected / exposed	0 / 630 (0.00%)	3 / 589 (0.51%)	4 / 256 (1.56%)
occurrences (all)	0	3	4
Illusion			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Impulse-control disorder			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Initial insomnia			

subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	1	1	1
Insomnia			
subjects affected / exposed	6 / 630 (0.95%)	13 / 589 (2.21%)	2 / 256 (0.78%)
occurrences (all)	6	13	2
Irritability			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	1 / 256 (0.39%)
occurrences (all)	0	2	1
Libido increased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Mania			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Mood altered			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Mood swings			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Nervousness			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Nightmare			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Panic disorder			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Rapid eye movement sleep			

behaviour disorder			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Rapid eye movements sleep abnormal			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Restlessness			
subjects affected / exposed	0 / 630 (0.00%)	4 / 589 (0.68%)	0 / 256 (0.00%)
occurrences (all)	0	4	0
Sleep disorder			
subjects affected / exposed	2 / 630 (0.32%)	5 / 589 (0.85%)	0 / 256 (0.00%)
occurrences (all)	2	5	0
Stereotypy			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Tearfulness			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Thinking abnormal			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Investigations			
Biopsy skin			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Blood creatinine increased			

subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Blood glucose increased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	1 / 630 (0.16%)	6 / 589 (1.02%)	2 / 256 (0.78%)
occurrences (all)	1	6	2
Blood sodium decreased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Computerised tomogram abnormal			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Coronavirus test positive			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Ejection fraction decreased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Electrocardiogram abnormal			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Electrocardiogram low voltage			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1

Lymphocyte count decreased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Oxygen saturation decreased			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
QRS axis abnormal			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Viral test negative			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	1 / 630 (0.16%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	1	2	0
White blood cells urine positive			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Exposure to toxic agent			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	6 / 630 (0.95%)	13 / 589 (2.21%)	5 / 256 (1.95%)
occurrences (all)	6	13	5
Foot fracture			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Hand fracture			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Joint dislocation			

subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	1 / 256 (0.39%)
occurrences (all)	0	2	1
Joint injury			
subjects affected / exposed	1 / 630 (0.16%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	1	2	0
Ligament sprain			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Limb injury			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Neck injury			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Post vaccination syndrome			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Procedural nausea			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Product administration error			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Radius fracture			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	1	0	1
Road traffic accident			

subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Spinal compression fracture			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Tooth fracture			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Upper limb fracture			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	2 / 256 (0.78%)
occurrences (all)	0	0	2
Atrioventricular block first degree			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block second degree			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Bundle branch block left			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0

Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Akinesia			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Anosognosia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Carpal tunnel syndrome			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	0	1	1
Cervicobrachial syndrome			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Depressed level of consciousness			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Disturbance in attention			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	3 / 630 (0.48%)	17 / 589 (2.89%)	6 / 256 (2.34%)
occurrences (all)	3	17	6
Dizziness postural			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Drooling			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Dysaesthesia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Dysarthria			

subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Dystonia			
subjects affected / exposed	2 / 630 (0.32%)	3 / 589 (0.51%)	2 / 256 (0.78%)
occurrences (all)	2	3	2
Freezing phenomenon			
subjects affected / exposed	0 / 630 (0.00%)	3 / 589 (0.51%)	2 / 256 (0.78%)
occurrences (all)	0	3	2
Headache			
subjects affected / exposed	8 / 630 (1.27%)	9 / 589 (1.53%)	3 / 256 (1.17%)
occurrences (all)	8	9	3
Hyperkinesia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Hypersomnia			
subjects affected / exposed	2 / 630 (0.32%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	2	1	1
Hypoaesthesia			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	2 / 256 (0.78%)
occurrences (all)	0	2	2
Judgement impaired			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Lethargy			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Memory impairment			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Migraine			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Migraine with aura			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Movement disorder			

subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	0	1	1
Muscle contractions involuntary			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Myoclonus			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Parkinson's disease			
subjects affected / exposed	1 / 630 (0.16%)	3 / 589 (0.51%)	2 / 256 (0.78%)
occurrences (all)	1	3	2
Parkinsonian rest tremor			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Parkinsonism			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Poor quality sleep			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	3 / 630 (0.48%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	3	0	1
Sciatica			
subjects affected / exposed	2 / 630 (0.32%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	2	0	1
Somnolence			

subjects affected / exposed	1 / 630 (0.16%)	5 / 589 (0.85%)	4 / 256 (1.56%)
occurrences (all)	1	5	4
Taste disorder			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	2 / 630 (0.32%)	3 / 589 (0.51%)	1 / 256 (0.39%)
occurrences (all)	2	3	1
Balance disorder			
subjects affected / exposed	1 / 630 (0.16%)	6 / 589 (1.02%)	2 / 256 (0.78%)
occurrences (all)	1	6	2
Dysphonia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Epilepsy			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	2 / 256 (0.78%)
occurrences (all)	1	0	2
Syncope			
subjects affected / exposed	1 / 630 (0.16%)	3 / 589 (0.51%)	1 / 256 (0.39%)
occurrences (all)	1	3	1
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	1	0	1
Vertigo positional			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	0	1	1
Eye disorders			

Accommodation disorder			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Cataract			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Eyelid ptosis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 630 (0.00%)	3 / 589 (0.51%)	1 / 256 (0.39%)
occurrences (all)	0	3	1
Visual impairment			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	2 / 256 (0.78%)
occurrences (all)	0	2	2
Abdominal pain upper			
subjects affected / exposed	0 / 630 (0.00%)	4 / 589 (0.68%)	0 / 256 (0.00%)
occurrences (all)	0	4	0
Aptyalism			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Breath odour			

subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Chapped lips			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	7 / 630 (1.11%)	12 / 589 (2.04%)	4 / 256 (1.56%)
occurrences (all)	7	12	4
Diarrhoea			
subjects affected / exposed	4 / 630 (0.63%)	5 / 589 (0.85%)	0 / 256 (0.00%)
occurrences (all)	4	5	0
Dry mouth			
subjects affected / exposed	2 / 630 (0.32%)	25 / 589 (4.24%)	3 / 256 (1.17%)
occurrences (all)	2	25	3
Dyspepsia			
subjects affected / exposed	2 / 630 (0.32%)	3 / 589 (0.51%)	1 / 256 (0.39%)
occurrences (all)	2	3	1
Dysphagia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Gastritis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	0	1	1
Hiatus hernia			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Impaired gastric emptying			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	7 / 630 (1.11%)	29 / 589 (4.92%)	11 / 256 (4.30%)
occurrences (all)	7	29	11
Oesophagitis			

subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Oral dysaesthesia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Post-tussive vomiting			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Retching			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Tooth loss			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	1	0	1
Vomiting			
subjects affected / exposed	3 / 630 (0.48%)	13 / 589 (2.21%)	3 / 256 (1.17%)
occurrences (all)	3	13	3
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Cold sweat			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Dermatitis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1

Hyperhidrosis			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	0 / 256 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	2 / 256 (0.78%)
occurrences (all)	0	2	2
Rash generalised			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Rash papular			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Hydronephrosis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Incontinence			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Micturition urgency			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Nocturia			

subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Pollakiuria			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Polyuria			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Renal cyst			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Renal impairment			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Urge incontinence			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Urinary incontinence			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	0	1	1
Urinary tract inflammation			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Thyroid mass			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	4 / 256 (1.56%)
occurrences (all)	0	1	4
Arthritis			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	1	1	1
Bursitis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	2 / 256 (0.78%)
occurrences (all)	0	0	2
Dupuytren's contracture			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Gouty arthritis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Intervertebral disc compression			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Intervertebral disc disorder			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Muscle rigidity			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 630 (0.00%)	5 / 589 (0.85%)	1 / 256 (0.39%)
occurrences (all)	0	5	1
Muscle twitching			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	2 / 256 (0.78%)
occurrences (all)	0	0	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0

Musculoskeletal discomfort			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 630 (0.00%)	2 / 589 (0.34%)	1 / 256 (0.39%)
occurrences (all)	0	2	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	2 / 630 (0.32%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	2	1	0
Neck pain			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	2 / 256 (0.78%)
occurrences (all)	1	1	2
Pain in extremity			
subjects affected / exposed	1 / 630 (0.16%)	3 / 589 (0.51%)	3 / 256 (1.17%)
occurrences (all)	1	3	3
Plantar fasciitis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Spinal pain			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Spinal stenosis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Synovial cyst			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Trismus			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Appendicitis			

subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Arthritis infective			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Balanitis candida			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	1	0	1
Cellulitis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Conjunctivitis bacterial			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Corona virus infection			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	3 / 256 (1.17%)
occurrences (all)	0	1	3
Folliculitis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Hordeolum			

subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 630 (0.48%)	7 / 589 (1.19%)	2 / 256 (0.78%)
occurrences (all)	3	7	2
Onychomycosis			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	1 / 256 (0.39%)
occurrences (all)	1	0	1
Oral herpes			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 630 (0.00%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	0	0	0
Rhinovirus infection			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Severe acute respiratory syndrome			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	1 / 630 (0.16%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 630 (0.32%)	2 / 589 (0.34%)	2 / 256 (0.78%)
occurrences (all)	2	2	2
Urinary tract infection			

subjects affected / exposed	1 / 630 (0.16%)	7 / 589 (1.19%)	4 / 256 (1.56%)
occurrences (all)	1	7	4
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	1 / 256 (0.39%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	2 / 630 (0.32%)	6 / 589 (1.02%)	0 / 256 (0.00%)
occurrences (all)	2	6	0
Dehydration			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Diabetes mellitus			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Gout			
subjects affected / exposed	0 / 630 (0.00%)	1 / 589 (0.17%)	0 / 256 (0.00%)
occurrences (all)	0	1	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 630 (0.16%)	0 / 589 (0.00%)	0 / 256 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	IR CD-LD Double-Blind Period		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 250 (31.60%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Extranodal marginal zone B-cell lymphoma (MALT type)			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Squamous cell carcinoma			

subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Vascular disorders			
Blood pressure inadequately controlled			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	3 / 250 (1.20%)		
occurrences (all)	3		
Hypertensive crisis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Hypertensive urgency			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Labile hypertension			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Orthostatic hypotension			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Peripheral venous disease			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Thrombosis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Varicophlebitis			

subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Balance disorder			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Chest discomfort			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Feeling abnormal			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Gait disturbance			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Hernia			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Mass			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Oedema			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Oedema peripheral			

subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Erectile dysfunction			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Prostatitis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Vaginal prolapse			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Dry throat			

subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Pulmonary mass			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Affect lability			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Agitation			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		

Anxiety				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Apathy				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Behaviour disorder				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Binge eating				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Bruxism				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Confusional state				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Depressed mood				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Depression				
subjects affected / exposed	2 / 250 (0.80%)			
occurrences (all)	2			
Fear				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hallucination				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hallucination, auditory				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hallucination, visual				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			

Illusion				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Impulse-control disorder				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Initial insomnia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Insomnia				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Irritability				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Libido increased				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Mania				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Mood altered				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Mood swings				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Nervousness				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Nightmare				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Obsessive-compulsive disorder				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			

Panic attack			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Panic disorder			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Rapid eye movement sleep behaviour disorder			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Rapid eye movements sleep abnormal			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Restlessness			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Stereotypy			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Tearfulness			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Thinking abnormal			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Investigations			
Biopsy skin			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			

subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Blood creatine phosphokinase increased				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Blood creatinine increased				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Blood glucose increased				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Blood pressure increased				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Blood sodium decreased				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Blood urea increased				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Computerised tomogram abnormal				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Coronavirus test positive				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Ejection fraction decreased				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Electrocardiogram abnormal				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Electrocardiogram low voltage				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			

Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	1 / 250 (0.40%) 1		
Electrocardiogram repolarisation abnormality subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Oxygen saturation decreased subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
QRS axis abnormal subjects affected / exposed occurrences (all)	1 / 250 (0.40%) 1		
Viral test negative subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Weight decreased subjects affected / exposed occurrences (all)	1 / 250 (0.40%) 1		
White blood cells urine positive subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Injury, poisoning and procedural complications			
Exposure to toxic agent subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Fall subjects affected / exposed occurrences (all)	9 / 250 (3.60%) 9		
Foot fracture subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Hand fracture			

subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Head injury				
subjects affected / exposed	2 / 250 (0.80%)			
occurrences (all)	2			
Joint dislocation				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Joint injury				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Ligament sprain				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Limb injury				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Meniscus injury				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Muscle strain				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Neck injury				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Post vaccination syndrome				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Procedural nausea				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Procedural pain				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Product administration error				

subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Radius fracture			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Road traffic accident			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Spinal compression fracture			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Tooth fracture			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Upper limb fracture			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Wrist fracture			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Atrioventricular block first degree			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Atrioventricular block second degree			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Bundle branch block left			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		

Palpitations			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Akinesia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Anosognosia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Carpal tunnel syndrome			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Cervicobrachial syndrome			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Depressed level of consciousness			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Disturbance in attention			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	2 / 250 (0.80%)		
occurrences (all)	2		
Dizziness postural			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Drooling			

subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Dysaesthesia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Dysarthria				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Dystonia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Freezing phenomenon				
subjects affected / exposed	2 / 250 (0.80%)			
occurrences (all)	2			
Headache				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hyperkinesia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hypersomnia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hypoaesthesia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Judgement impaired				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Lethargy				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Memory impairment				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Migraine				

subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Migraine with aura				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Movement disorder				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Muscle contractions involuntary				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Myoclonus				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Neuropathy peripheral				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Paraesthesia				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Parkinson's disease				
subjects affected / exposed	2 / 250 (0.80%)			
occurrences (all)	2			
Parkinsonian rest tremor				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Parkinsonism				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Poor quality sleep				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Presyncope				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Restless legs syndrome				

subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	2 / 250 (0.80%)		
occurrences (all)	2		
Taste disorder			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	2 / 250 (0.80%)		
occurrences (all)	2		
Balance disorder			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Epilepsy			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Vertigo			

subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Vertigo positional			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Eye disorders			
Accommodation disorder			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Cataract			
subjects affected / exposed	2 / 250 (0.80%)		
occurrences (all)	2		
Dry eye			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Eyelid ptosis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Abdominal distension			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			

subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Aptyalism				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Breath odour				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Chapped lips				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Diarrhoea				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Dry mouth				
subjects affected / exposed	2 / 250 (0.80%)			
occurrences (all)	2			
Dyspepsia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Gastritis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hiatus hernia				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Impaired gastric emptying				

subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	2 / 250 (0.80%)		
occurrences (all)	2		
Oesophagitis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Oral dysaesthesia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Post-tussive vomiting			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Retching			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Tooth loss			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Cold sweat			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		

Dry skin subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Erythema subjects affected / exposed occurrences (all)	1 / 250 (0.40%) 1		
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Rash subjects affected / exposed occurrences (all)	2 / 250 (0.80%) 2		
Rash generalised subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Rash papular subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Skin ulcer subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Haematuria subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Hydronephrosis subjects affected / exposed occurrences (all)	1 / 250 (0.40%) 1		
Incontinence			

subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Micturition urgency			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Nocturia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Polyuria			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Renal cyst			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Renal impairment			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Urge incontinence			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Urinary incontinence			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Urinary tract inflammation			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		

Thyroid mass			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Arthritis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Bursitis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Dupuytren's contracture			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Gouty arthritis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Intervertebral disc compression			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Intervertebral disc disorder			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Muscle rigidity			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Muscle twitching			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Muscular weakness			

subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Musculoskeletal discomfort				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Musculoskeletal pain				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Musculoskeletal stiffness				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Myalgia				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Neck pain				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Pain in extremity				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Plantar fasciitis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Spinal pain				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Spinal stenosis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Synovial cyst				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Trismus				

subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Arthritis infective			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Balanitis candida			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Conjunctivitis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Conjunctivitis bacterial			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Corona virus infection			
subjects affected / exposed	1 / 250 (0.40%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		
Gastroenteritis viral			
subjects affected / exposed	0 / 250 (0.00%)		
occurrences (all)	0		

Herpes zoster				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Localised infection				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	2 / 250 (0.80%)			
occurrences (all)	2			
Onychomycosis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Rhinovirus infection				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Severe acute respiratory syndrome				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			
Tooth abscess				
subjects affected / exposed	1 / 250 (0.40%)			
occurrences (all)	1			
Tooth infection				
subjects affected / exposed	0 / 250 (0.00%)			
occurrences (all)	0			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 250 (1.20%) 3		
Urinary tract infection subjects affected / exposed occurrences (all)	8 / 250 (3.20%) 8		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Metabolism and nutrition disorders Appetite disorder subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Decreased appetite subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Dehydration subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Diabetes mellitus subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Gout subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	0 / 250 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2017	Protocol amendment 1: • Changed the IR CD-LD package insert provided in Appendix A from carbidopa and levodopa tablets (Mylan Pharmaceuticals Inc.) to Sinemet® (carbidopa-levodopa) tablets (Merck & Co., Inc.). • Added the following statement to the IR CD-LD dose adjustment period, Section 6.4.1 'Subjects who were receiving IR CD-LD as a 1:10 CD-LD formulation will be started on IR CD-LD with a 1:4 ratio at the same frequency and LD dose.' • Added a new section on Rescue Medications as follows: Subjects who need rescue medications or need to change treatment will be discontinued from the study. Rescue with additional or modified doses of concomitant PD medications or use of CD-LD products other than the dispensed study medication are not permitted and will trigger discontinuation from the study. Rescue medications are not allowed during the dose adjustment, dose conversion or double-blind treatment periods. • Updated the third key secondary endpoint as follows: Change from baseline in the MDS-UPDRS Part III at end of double-blind treatment period (Visit 7 or early termination).
23 October 2017	Protocol amendment 2: • To clarify the dose adjustments made during the dose adjustment period: Following Visit 1, qualified subjects will enter a 3-week, open-label IR CD-LD treatment period allowing for dose adjustment. 'The dosing regimen of IR CD-LD may be adjusted during the dose adjustment period to minimize "Off" time without causing troublesome dyskinesia. The doses and regimens of the subject's other non-CD-LD PD medications (dopamine agonists, MAO-B inhibitors, amantadine, anticholinergics) should remain stable throughout this study.' • To clarify the dose conversion made during the dose conversion period: Following completion of the IR CD-LD dose adjustment period…… It is recommended that IPX203 should be dosed approximately every 8 hours with the exception that subjects who are currently receiving a total daily dose of less than 125-500 mg IR CD-LD at the end of the dose adjustment period will be initially administered every 12 hours. The dosing interval may be reduced to approximately every 8 hours if the subject does not achieve an acceptable duration of effect. The dosing regimen of IPX203 may be adjusted during the dose conversion period to achieve the optimal balance of efficacy and tolerability (minimize "Off" time without causing troublesome dyskinesia or other dopaminergic side effects). The doses and regimens of the subject's other non-CD-LD PD medications should remain stable throughout this study. The subject must be on a stable dosing regimen of IPX203 (no change in dose or in dosing frequency) for at least 5 days prior to returning for Visit 4. • During the dose conversion to IPX203, the Investigator or site staff are advised to be in frequent contact (every 1 to 3 days) with the subject especially during the initial dose conversion to assess the need for dosage adjustment with the goal of minimizing "Off" time without causing troublesome dyskinesia.
07 December 2017	Protocol amendment 3: • Included the maximum recommended daily dose of IPX203 in Dose Conversion Period as 600 to 2400 mg CD-LD.
28 September 2018	Protocol amendment 4: • Updated the measures and/or instruments such as MDS-UPDRS, PDQ-39, GCSI, PDSS-2, PAS, PD Diary to the most current versions available for licensing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported