Clinical trial results:
Efficacy and Safety of Eslicarbazepine Acetate (Bia 2-093) as Adjunctive Therapy for Refractory Partial Seizures in a Double-Blind, Randomized, Placebo-Controlled, Parallel-Group, Multicentre Clinical Trial

Summary

EudraCT number	2008-002455-25
Trial protocol	FR IT DE GR CY HU RO
Global end of trial date	16 May 2018

Results information

Result version number	v3 (current)
This version publication date	03 July 2021
First version publication date	20 April 2016
Version creation reason	
Summary attachment (see zip file)	BIA-2093-304 Synopsis (BIA-2093-304 Synopsis.pdf) amendment (bial-bia-2093-3045-synopsis-report.pdf)

Trial information

Trial identification

Sponsor protocol code	BIA-2093-304

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	BIAL - Portela & CA, S.A.
Sponsor organisation address	À Av. Siderurgia Nacional, Coronado, Portugal, 4745-457
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 March 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 January 2012
Global end of trial reached?	Yes
Global end of trial date	16 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary: To evaluate the efficacy of Eslicarbazepine acetate (ESL) administered once daily (QD) at doses of 800 mg and 1200 mg compared with placebo as adjunctive therapy in patients with refractory partial epilepsy over a 12-week maintenance period. The primary objective was evaluated in Part I of the study and is reported in the Part I Clinical Study Report (CSR).
Secondary: The secondary objectives evaluated in Part II and Part III were:
- To evaluate the safety and tolerability of ESL at doses titrated to an efficacy or safety endpoint over a 1-year open-label period (Part II).
- To assess the maintenance of therapeutic effects of ESL over a 1-year open-label period (Part II).
- To assess the drug-drug pharmacokinetic (PK) interactions between ESL and concomitant anti-epileptic drugs (AEDs) in Part II of the study.
- To assess the health-related quality-of-life and depressive symptoms in Part II of the study.
- To study the effects of long-term use of ESL in Part III of the

Protection of trial subjects:

This study was conducted in compliance with the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Good
Clinical Practice, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 43
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Brazil: 111
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Cyprus: 7
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	Greece: 12
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	India: 91
Country: Number of subjects enrolled	Italy: 33
Country: Number of subjects enrolled	Korea, Republic of: 85

Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Romania: 26
Country: Number of subjects enrolled	Turkey: 4
Country: Number of subjects enrolled	Ukraine: 60
Country: Number of subjects enrolled	United States: 365
Country: Number of subjects enrolled	South Africa: 15
Worldwide total number of subjects	936
EEA total number of subjects	143

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	19
Adults (18-64 years)	896
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 615 patients in approximately 200 sites within Argentina, Australia, Brazil, Belgium, Canada, Cyprus, France, Germany, Greece, Hungary, India, Italy, Poland, Russia, Turkey, South Korea, Romania, South Africa, Ukraine and the United States needed. Recruitment closed as soon as the required number of randomised patients was achieved.

Pre-assignment

Screening details:

Subjects who met all the inclusion criteria and none of the exclusion criteria. 936 subjects were screened. For283 subjects were stated Screen Failure, 653 subjects were randomised.

Pre-assignment period milestones

Number of subjects started	936
Number of subjects completed	653

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Adverse event, serious non-fatal: 10
Reason: Number of subjects	Consent withdrawn by subject: 31
Reason: Number of subjects	Physician decision: 2
Reason: Number of subjects	Protocol deviation: 202
Reason: Number of subjects	Lack of Efficacy: 1
Reason: Number of subjects	Sponsor's decision: 2
Reason: Number of subjects	Patient Non-Compliance: 14
Reason: Number of subjects	Missing: 3
Reason: Number of subjects	Other: 17

Period 1

Period 1 title	Part I: double-blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Part I - Placebo

Arm description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with placebo QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received placebo QD.
After maintenance subjects were down-titraded by receiving placebo QD for 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo tablets QD orally during Part 1, the 2-week, double-blind, up-titration period (Week 1 to Week 2), and the 12-week double-blind maintenance period (Week 3 to Week 14). All patients received ESL in Part II and Part III. For Part II and Part III, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In Part II, the starting dose had to be kept stable at 800 mg QD for 1 month. After that titration upwards or downwards was done at 400 mg increments by Investigator's judgement. Maximum dose allowed was 1600 mg QD and the minimum dose was 400 mg QD. In additional open-label extension Part III, patients started with Part II dose with the option to titrate this dose within a 400−1600 mg QD dose range, in no more than 400 increments. If not entering Part III down-titration in dependance of last dose level was done.

Arm title	Part I - Eslicarbazepine Acetate 800 mg

Arm description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with ESL 400 mg QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received ESL 800 mg QD.
After maintenance subjects were down-titraded to 400 mg for a duration of 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Arm type	Active comparator
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

800 mg tablets QD orally during Part 1, the 2-week, double-blind, up-titration period (Week 1 to Week 2), and the 12-week double-blind maintenance period (Week 3 to Week 14). For Part II and Part III, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In Part II, the starting dose had to be kept stable at 800 mg QD for 1 month. After that titration upwards or downwards was done at 400 mg increments by Investigator's judgement. Maximum dose allowed was 1600 mg QD and the minimum dose was 400 mg QD. In additional open-label extension Part III, patients started with Part II dose with the option to titrate this dose within a 400−1600 mg QD dose range, in no more than 400 increments. If not entering Part III down-titration in dependance of last dose level was done (see synopsis).

Arm title	Part I - Eslicarbazepine Acetate 1200 mg

Arm description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with ESL 800 mg QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received ESL 120 mg QD.
After maintenance subjects were down-titraded to 800 mg for a duration of 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Arm type	Active comparator

Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

800 mg and 400 mg tablets QD orally during Part 1, the 2-week, double-blind, up-titration period (Week 1 to Week 2), and the 12-week double-blind maintenance period (Week 3 to Week 14). For Part II and Part III, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In Part II, the starting dose had to be kept stable at 800 mg QD for 1 month. After that titration upwards or downwards was done at 400 mg increments by Investigator's judgement. Maximum dose allowed was 1600 mg QD and the minimum dose was 400 mg QD. In additional open-label extension Part III, patients started with Part II dose with the option to titrate this dose within a 400−1600 mg QD dose range, in no more than 400 increments. If not entering Part III down-titration in dependance of last dose level was done (see synopsis).

Number of subjects in period 1[1]	Part I - Placebo	Part I - Eslicarbazepine Acetate 800 mg	Part I - Eslicarbazepine Acetate 1200 mg
Started	226	216	211
Completed	189	173	142
Not completed	37	43	69
Sponsor's decision	1	2	1
Consent withdrawn by subject	7	7	12
Physician decision	1	-	3
Lack of Efficacy	-	-	1
Adverse event, non-fatal	9	20	44
Patient Non-Compliance	5	1	3
Other	8	8	1
Pregnancy	2	1	-
Adverse event, serious non-fatal	-	1	1
Protocol deviation	4	3	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: During observation pretime, 653 of 936 subjects enrolled turned out to be eligible for randomisation and started part I.

Period 2

Period 2 title	Part II: one-year open-label extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Part II - Placebo

Arm description:

patients who completed placebo treatment in Part I and were willing to participate in the extension part Part II respectively

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

For Part II, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In Part II, the starting dose had to be kept stable at 800 mg QD for 1 month. After that titration upwards or downwards was done at 400 mg increments by Investigator’s judgement. Maximum dose allowed was 1600 mg QD and the minimum dose was 400 mg QD.

Arm title	Part II - Eslicarbazepine Acetate 800 mg

Arm description:

patients who completed ESL 800 mg QD treatment in Part I and were willing to participate in the extension part Part II respectively

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

For Part II, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In Part II, the starting dose had to be kept stable at 800 mg QD for 1 month. After that titration upwards or downwards was done at 400 mg increments by Investigator’s judgement. Maximum dose allowed was 1600 mg QD and the minimum dose was 400 mg QD.

Arm title	Part II - Eslicarbazepine Acetate 1200 mg

Arm description:

patients who completed ESL 1200 mg QD treatment in Part I and were willing to participate in the extension part Part II respectively

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

For Part II, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In Part II, the starting dose had to be kept stable at 800 mg QD for 1 month. After that titration upwards or downwards was done at 400 mg increments by Investigator’s judgement. Maximum dose allowed was 1600 mg QD and the minimum dose was 400 mg QD.

Number of subjects in period 2[2]	Part II - Placebo	Part II - Eslicarbazepine Acetate 800 mg	Part II - Eslicarbazepine Acetate 1200 mg
Started	186	170	140
Completed	118	127	101
Not completed	68	43	39
Sponsor's decision	3	2	2
Consent withdrawn by subject	22	13	11
Physician decision	3	2	2
Lack of Efficacy	3	1	2
Adverse event, non-fatal	15	3	5
Other	17	18	16
Pregnancy	2	1	-
Adverse event, serious non-fatal	3	2	1
Protocol deviation	-	1	-

Notes:

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

Justification: The prerequisite for participating in Part II was the completion of Part I. In addition, separate consent from the subject was required. 496 of 504 completers of Part I gave their consent to participate in Part II.

Period 3

Period 3 title	Part III: open-label additioal extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Part III - Placebo

Arm description:

patients who completed placebo treatment in Part I, completed Part II and were willing to participate in the extension part Part III respectively

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

For Part III, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In additional open-label extension Part III, patients started with Part II dose with the option to titrate this dose within a 400−1600 mg QD dose range, in no more than 400 increments. If not entering Part III down-titration in dependance of last dose level was done (see synopsis).

Arm title	Part III - Eslicarbazepine Acetate 800 mg

Arm description:

patients who completed ESL 800 mg QD treatment in Part I, completed Part II and were willing to participate in the extension part Part III respectively

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

For Part III, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In additional open-label extension Part III, patients started with Part II dose with the option to titrate this dose within a 400−1600 mg QD dose range, in no more than 400 increments. If not entering Part III down-titration in dependance of last dose level was done (see synopsis).

Arm title	Part III - Eslicarbazepine Acetate 1200 mg

Arm description:

patients who completed ESL 1200 mg QD treatment in Part I, completed Part II and were willing to participate extension part Part III respectively

Arm type	Experimental
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

For Part III, scored 800 mg tablets will be supplied. The tablets were taken QD by mouth, swallowed at approximately the same time each day, Patients were instructed not to chew or crush the study medication. In additional open-label extension Part III, patients started with Part II dose with the option to titrate this dose within a 400−1600 mg QD dose range, in no more than 400 increments. If not entering Part III down-titration in dependance of last dose level was done (see synopsis).

Number of subjects in period 3[3]	Part III - Placebo	Part III - Eslicarbazepine Acetate 800 mg	Part III - Eslicarbazepine Acetate 1200 mg
Started	78	87	75
Completed	20	18	17
Not completed	58	69	58
Sponsor's decision	11	8	12
Consent withdrawn by subject	10	18	14
Physician decision	1	4	3
Lack of Efficacy	1	1	-
Adverse event, non-fatal	3	3	-
Other	31	34	27
Pregnancy	-	-	1
Adverse event, serious non-fatal	1	-	-
Missing	-	1	-
Protocol deviation	-	-	1

Notes:

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

Justification: The prerequisite for participating in Part III was the completion of Part II. In addition, separate consent from the subject was required. 240 of 346 completers of Part II gave their consent to participate in Part III.

Baseline characteristics

Reporting groups	
Reporting group title	Part I - Placebo

Reporting group description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with placebo QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received placebo QD.
After maintenance subjects were down-titraded by receiving placebo QD for 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Reporting group title	Part I - Eslicarbazepine Acetate 800 mg

Reporting group description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with ESL 400 mg QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received ESL 800 mg QD.
After maintenance subjects were down-titraded to 400 mg for a duration of 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Reporting group title	Part I - Eslicarbazepine Acetate 1200 mg

Reporting group description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with ESL 800 mg QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received ESL 120 mg QD.
After maintenance subjects were down-titraded to 800 mg for a duration of 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Reporting group values	Part I - Placebo	Part I - Eslicarbazepine Acetate 800 mg	Part I - Eslicarbazepine Acetate 1200 mg
Number of subjects	226	216	211
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	0
Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days – 23months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 year)	5	4	6
From 18 - 64 years	217	207	203
From 65 – 84 years	3	5	2
Over 85 years	0	0	0
Missing	1	0	0

Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean	39.1	38.8	38.0
standard deviation	± 12.71	± 12.11	± 11.98
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	114	109	106
Male	112	107	105

Reporting group values	Total		
Number of subjects	653		
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0		
Preterm newborn- gestational age < 37 wk	0		
Newborns (0-27days)	0		
Infants and toddlers (28days – 23months)	0		
Children (2-11 years)	0		
Adolescents (12-17 year)	15		
From 18 - 64 years	627		
From 65 – 84 years	10		
Over 85 years	0		
Missing	1		
Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	329		
Male	324		

End points

End points reporting groups

Reporting group title	Part I - Placebo

Reporting group description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with placebo QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received placebo QD.
After maintenance subjects were down-titraded by receiving placebo QD for 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Reporting group title	Part I - Eslicarbazepine Acetate 800 mg

Reporting group description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with ESL 400 mg QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received ESL 800 mg QD.
After maintenance subjects were down-titraded to 400 mg for a duration of 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Reporting group title	Part I - Eslicarbazepine Acetate 1200 mg

Reporting group description:

Age ≥16
8-week observation baseline period (Week -8 to Week -1), randomization of eligible subjects at the end of the 8-week observational baseline period.
2-week, double-blind, up-titration period (Week 1 to Week 2) with ESL 800 mg QD.
12-week, double-blind, maintenance period (Week 3 to Week 14), where subjects received ESL 120 mg QD.
After maintenance subjects were down-titraded to 800 mg for a duration of 2 weeks if not entered Part II.
Concomitant AEDs were allowed in this study and were to be kept stable during the course of the study.

Reporting group title	Part II - Placebo

Reporting group description:

patients who completed placebo treatment in Part I and were willing to participate in the extension part Part II respectively

Reporting group title	Part II - Eslicarbazepine Acetate 800 mg

Reporting group description:

patients who completed ESL 800 mg QD treatment in Part I and were willing to participate in the extension part Part II respectively

Reporting group title	Part II - Eslicarbazepine Acetate 1200 mg

Reporting group description:

patients who completed ESL 1200 mg QD treatment in Part I and were willing to participate in the extension part Part II respectively

Reporting group title	Part III - Placebo

Reporting group description:

patients who completed placebo treatment in Part I, completed Part II and were willing to participate in the extension part Part III respectively

Reporting group title	Part III - Eslicarbazepine Acetate 800 mg

Reporting group description:

patients who completed ESL 800 mg QD treatment in Part I, completed Part II and were willing to participate in the extension part Part III respectively

Reporting group title	Part III - Eslicarbazepine Acetate 1200 mg

Reporting group description:

patients who completed ESL 1200 mg QD treatment in Part I, completed Part II and were willing to participate extension part Part III respectively

Subject analysis set title	Part I - Placebo x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized subjects who received at least one dose of study drug after randomization

Subject analysis set title	Part I - Eslicarbazepine Acetate 800 mg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized subjects who received at least one dose of study drug after randomization

Subject analysis set title	Part I - Eslicarbazepine Acetate 1200 mg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized subjects who received at least one dose of study drug after randomization

Subject analysis set title	Part I - Placebo x Intent-to-treat Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomized subjects who received at least one dose of study drug after randomization and had at least one post-baseline seizure frequency assessment

Subject analysis set title	Part I - Eslicarbazepine Acetate 800 mg x Intent-to-treat Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomized subjects who received at least one dose of study drug after randomization and had at least one post-baseline seizure frequency assessment

Subject analysis set title	Part I - Eslicarbazepine Acetate 1200 mg x Intent-to-treat Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All randomized subjects who received at least one dose of study drug after randomization and had at least one post-baseline seizure frequency assessment

Subject analysis set title	Part I - Placebo x DE ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the ITT population who completed the DE diary

Subject analysis set title	Part I - Eslicarbazepine Acetate 800 mg x DE ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the ITT population who completed the DE diary

Subject analysis set title	Part I - Eslicarbazepine Acetate 1200 mg x DE ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the ITT population who completed the DE diary

Subject analysis set title	Part I - Placebo x EE ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the ITT population who completed the EE diary

Subject analysis set title	Part I - Eslicarbazepine Acetate 800 mg x EE ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the ITT population who completed the EE diary

Subject analysis set title	Part I - Eslicarbazepine Acetate 1200 mg x EE ITT Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects in the ITT population who completed the EE diary

Subject analysis set title	Part I - Placebo x Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:
All subjects in ITT population without any important protocol deviation

Subject analysis set title	Part I - Eslicarbazepine Acetate 800 mg x Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:
All subjects in ITT population without any important protocol deviation

Subject analysis set title	Part I - Eslicarbazepine Acetate 1200 mg x Per Protocol Set
Subject analysis set type	Per protocol

Subject analysis set description:
All subjects in ITT population without any important protocol deviation

Subject analysis set title	Part II - Placebo x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:
All patients in Part I Safety population who entered Part II

Subject analysis set title	Part II - Eslicarbazepine Acetate 800 mg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:
All patients in Part I Safety population who entered Part II

Subject analysis set title	Part II - Eslicarbazepine Acetate 1200 mg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:
All patients in Part I Safety population who entered Part II

Subject analysis set title	Part III - Placebo x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:
All patients in Part I Safety population who entered Part III

Subject analysis set title	Part III - Eslicarbazepine Acetate 800 mg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:
All patients in Part I Safety population who entered Part III

Subject analysis set title	Part III - Eslicarbazepine Acetate 1200 mg x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:
All patients in Part I Safety population who entered Part III

Primary: Standardized Seizure Frequency During the Maintenance Period

End point title	Standardized Seizure Frequency During the Maintenance Period

End point description:
Mean

End point type	Primary

End point timeframe:
During the Maintenance Period

End point values	Part I - Placebo x Intent-to-treat Set	Part I - Eslicarbazepine Acetate 800 mg x Intent-to-treat Set	Part I - Eslicarbazepine Acetate 1200 mg x Intent-to-treat Set	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	212	200	184	
Units: Seizures				
number (not applicable)				
Seizures	12.99	13.7	12.05	

Statistical analyses

Statistical analysis title	ANCOVA analysis, ITT pop. strat by treatment.

Statistical analysis description:

Results are based on an ANCOVA model with log-transformed baseline standardized frequency and diary version as covariates and treatment as a fixed effect. The pairwise comparisons are each ESL dose versus placebo. LS means and CIs are back-transformed via the exponential function and subtracting 0.333. SEs for LS means are back-transformed via the Delta Method. Subjects who discontinued from the study during the titration period are not included.

Comparison groups	Part I - Placebo x Intent-to-treat Set v Part I - Eslicarbazepine Acetate 800 mg x Intent-to-treat Set
Number of subjects included in analysis	412
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	ANCOVA

Statistical analysis title	ANCOVA analysis, ITT pop. strat by treatment.

Statistical analysis description:

Results are based on an ANCOVA model with log-transformed baseline standardized frequency and diary version as covariates and treatment as a fixed effect. The pairwise comparisons are each ESL dose versus placebo. LS means and CIs are back-transformed via the exponential function and subtracting 0.333. SEs for LS means are back-transformed via the Delta Method. Subjects who discontinued from the study during the titration period are not included.

Comparison groups	Part I - Placebo x Intent-to-treat Set v Part I - Eslicarbazepine Acetate 1200 mg x Intent-to-treat Set
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From informed consent until the date of the EOT visit/EDV.

Adverse event reporting additional description:

AEs monitored at each visit from V1 throughout the study (including at early discontinuation and at the PSV). The investigator inquired generally about the patient's well being since the last visit. Details of any reported AEs were recorded at all scheduled and unscheduled visits as well as those reported during any telephone contact.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Placebo x Safety Set

Reporting group description:

Subjects in the Safety Set treated with Placebo

Reporting group title	Eslicarbazepine Acetate 800 mg x Safety Set

Reporting group description:

Subjects in the Safety Set treated with ESL

Reporting group title	Eslicarbazepine Acetate 1200 mg x Safety Set

Reporting group description:

Subjects in the Safety Set treated with ESL

Serious adverse events	Placebo x Safety Set	Eslicarbazepine Acetate 800 mg x Safety Set	Eslicarbazepine Acetate 1200 mg x Safety Set
Total subjects affected by serious adverse events			
subjects affected / exposed	33 / 226 (14.60%)	42 / 216 (19.44%)	29 / 211 (13.74%)
number of deaths (all causes)	1	3	2
number of deaths resulting from adverse events	1	3	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Cerebellar tumour			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Parathyroid tumour benign			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Arterial haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Hypotension			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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			
Sudden unexplained death in epilepsy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 2
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute psychosis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Affective disorder			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Agitation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Hallucination, auditory			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mood altered			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			

subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Anticonvulsant drug level below therapeutic			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood chloride decreased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood urea decreased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood urea nitrogen/creatinine ratio decreased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Drug level decreased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Cervical vertebral fracture			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Extradural haematoma			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Facial bones fracture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Femoral neck fracture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Femur fracture			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Joint dislocation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Ligament rupture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Near drowning			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Overdose			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Stab wound			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Therapeutic agent toxicity			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Congenital anomaly			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Mitral valve prolapse			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebellar syndrome			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Complex partial seizures			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Dizziness			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Encephalopathy			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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	2 / 226 (0.88%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Migraine			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Myoclonus			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Partial seizures			

subjects affected / exposed	2 / 226 (0.88%)	6 / 216 (2.78%)	6 / 211 (2.84%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures with secondary generalisation			
subjects affected / exposed	1 / 226 (0.44%)	6 / 216 (2.78%)	2 / 211 (0.95%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postictal state			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Simple partial seizures			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Somnolence			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	3 / 211 (1.42%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Leukocytosis			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall haematoma			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Dental caries			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Gastritis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Peritonitis			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Umbilical hernia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Vomiting			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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 and subcutaneous tissue disorders			
Leukocytoclastic vasculitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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 failure			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Appendicitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Bronchitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Disseminated tuberculosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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

Empyema			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Hepatitis C			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Malaria			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (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
Pelvic abscess			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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 / 226 (0.00%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Urosepsis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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
Vaginal abscess			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (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	3 / 226 (1.33%)	3 / 216 (1.39%)	0 / 211 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo x Safety Set	Eslicarbazepine Acetate 800 mg x Safety Set	Eslicarbazepine Acetate 1200 mg x Safety Set
Total subjects affected by non-serious adverse events			
subjects affected / exposed	193 / 226 (85.40%)	184 / 216 (85.19%)	196 / 211 (92.89%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acrochordon			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Angiofibroma			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Angiomyolipoma			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Basal cell carcinoma			

subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Benign neoplasm			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Breast cancer			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Cervicitis human papilloma virus			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Haemangioma of skin			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Uterine leiomyoma			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Carotidynia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Diastolic hypertension			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	1	1	2
Haematoma			
subjects affected / exposed	0 / 226 (0.00%)	4 / 216 (1.85%)	1 / 211 (0.47%)
occurrences (all)	0	5	2
Hot flush			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	5	1	0

Hyperaemia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	8 / 226 (3.54%)	4 / 216 (1.85%)	7 / 211 (3.32%)
occurrences (all)	13	5	15
Hypertensive crisis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	2
Hypotension			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	2 / 211 (0.95%)
occurrences (all)	1	2	3
Labile blood pressure			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Orthostatic hypotension			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Peripheral coldness			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Varicose vein			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Varicose vein ruptured			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Venous insufficiency			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Suture insertion			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	3	1	0
Asthenia			
subjects affected / exposed	7 / 226 (3.10%)	9 / 216 (4.17%)	11 / 211 (5.21%)
occurrences (all)	11	16	12
Chest discomfort			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	2	1	1
Chest pain			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	2	0	3
Chills			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Drug intolerance			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Facial pain			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	21 / 226 (9.29%)	10 / 216 (4.63%)	20 / 211 (9.48%)
occurrences (all)	28	20	32
Feeling abnormal			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Feeling drunk			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Feeling hot			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	3
Feeling jittery			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Gait disturbance			
subjects affected / exposed	6 / 226 (2.65%)	4 / 216 (1.85%)	4 / 211 (1.90%)
occurrences (all)	7	4	4
Generalised oedema			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Hyperthermia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Implant site pain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Inflammation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	2
Influenza like illness			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	2	1	2
Injection site reaction			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Irritability			
subjects affected / exposed	4 / 226 (1.77%)	5 / 216 (2.31%)	3 / 211 (1.42%)
occurrences (all)	7	9	4
Malaise			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Non-cardiac chest pain			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Oedema			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	5
Oedema peripheral			
subjects affected / exposed	3 / 226 (1.33%)	3 / 216 (1.39%)	4 / 211 (1.90%)
occurrences (all)	9	4	5
Pain			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	3	1	3
Pyrexia			
subjects affected / exposed	9 / 226 (3.98%)	6 / 216 (2.78%)	5 / 211 (2.37%)
occurrences (all)	12	10	6
Sluggishness			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Thirst			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	2	4	0
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Allergy to animal			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Hypersensitivity			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	1	2	2
Seasonal allergy			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	2	0	2
Social circumstances			
Physical assault			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	2
Breast cyst			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Breast disorder			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Cervical dysplasia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	5	0	2
Cervix haemorrhage uterine			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Dysmenorrhoea			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	1	1	3
Ejaculation disorder			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Epididymitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Erectile dysfunction			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	5	0	0
Fibrocystic breast disease			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Galactorrhoea			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Gynaecomastia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Menorrhagia			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Menstruation delayed			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Menstruation irregular			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Metrorrhagia			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Ovarian cyst			
subjects affected / exposed	2 / 226 (0.88%)	3 / 216 (1.39%)	0 / 211 (0.00%)
occurrences (all)	4	4	0
Pelvic pain			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Prostatitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Vaginal cyst			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Vaginal inflammation			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Varicocele			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	3 / 211 (1.42%)
occurrences (all)	0	0	3
Atelectasis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Bronchospasm			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	6 / 226 (2.65%)	6 / 216 (2.78%)	4 / 211 (1.90%)
occurrences (all)	7	7	5
Dyspnoea			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	4 / 211 (1.90%)
occurrences (all)	4	1	5
Dyspnoea exertional			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Emphysema			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	2	1
Epistaxis			

subjects affected / exposed	4 / 226 (1.77%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	4	2	1
Hiccups			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Lung disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	3 / 226 (1.33%)	4 / 216 (1.85%)	0 / 211 (0.00%)
occurrences (all)	3	6	0
Oropharyngeal pain			
subjects affected / exposed	3 / 226 (1.33%)	2 / 216 (0.93%)	2 / 211 (0.95%)
occurrences (all)	3	3	3
Paranasal sinus hypersecretion			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	2	1	2
Pharyngeal oedema			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Pneumonia aspiration			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Pulmonary congestion			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	2 / 211 (0.95%)
occurrences (all)	0	2	5
Rhinorrhoea			

subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Sinus congestion			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	1	4	0
Sleep apnoea syndrome			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	3	1	0
Snoring			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Throat tightness			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Abnormal dreams			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	4 / 211 (1.90%)
occurrences (all)	0	0	5
Affective disorder			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Aggression			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	2	1	3
Agitation			
subjects affected / exposed	2 / 226 (0.88%)	4 / 216 (1.85%)	1 / 211 (0.47%)
occurrences (all)	3	5	1
Anger			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	12 / 226 (5.31%)	18 / 216 (8.33%)	6 / 211 (2.84%)
occurrences (all)	17	32	16

Apathy			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	3	0	1
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	2
Bradyphrenia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Bruxism			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Communication disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Confusional state			
subjects affected / exposed	4 / 226 (1.77%)	2 / 216 (0.93%)	2 / 211 (0.95%)
occurrences (all)	5	4	2
Conversion disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Daydreaming			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 226 (0.00%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	0	4	3
Depression			
subjects affected / exposed	11 / 226 (4.87%)	10 / 216 (4.63%)	11 / 211 (5.21%)
occurrences (all)	23	13	19
Disorientation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Emotional disorder			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Flat affect			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Hallucination, visual			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Inappropriate affect			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Initial insomnia			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	3	0	1
Insomnia			
subjects affected / exposed	7 / 226 (3.10%)	8 / 216 (3.70%)	7 / 211 (3.32%)
occurrences (all)	11	9	9
Intermittent explosive disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Laziness			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Libido decreased			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	3	2	0
Libido increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Mental status changes			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Mood altered			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	0	1	2
Mood swings			

subjects affected / exposed	2 / 226 (0.88%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	2	6	3
Negative thoughts			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Nervousness			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	2	2	1
Nightmare			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Panic attack			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Panic disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Phonophobia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Postictal psychosis			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	0	4	0
Rapid eye movements sleep abnormal			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	3
Restlessness			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Self esteem decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0

Sleep disorder			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Social avoidant behaviour			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Somnambulism			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	2
Staring			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Stress			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Suicidal behaviour			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Suicidal ideation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	1	0	2
Suspiciousness			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	3 / 211 (1.42%)
occurrences (all)	1	3	4
Ammonia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	3 / 211 (1.42%)
occurrences (all)	3	2	3
Bacterial test positive			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Blood 1,25-dihydroxycholecalciferol decreased			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	4	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	3	0	2
Blood bilirubin increased			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	4	0	0
Blood chloride decreased			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Blood cholesterol increased			
subjects affected / exposed	4 / 226 (1.77%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	7	4	0
Blood creatine increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 226 (2.21%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	7	4	2
Blood creatinine increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	2	0	1
Blood iron decreased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Blood parathyroid hormone decreased			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	0	4	0
Blood parathyroid hormone increased			

subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	2	5	2
Blood phosphorus increased			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Blood potassium decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Blood potassium increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Blood pressure diastolic increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	3	0
Blood pressure systolic increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Blood sodium decreased			
subjects affected / exposed	4 / 226 (1.77%)	4 / 216 (1.85%)	5 / 211 (2.37%)
occurrences (all)	4	6	5
Blood testosterone decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	3 / 226 (1.33%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	5	3	2
Blood triglycerides increased			

subjects affected / exposed	3 / 226 (1.33%)	3 / 216 (1.39%)	1 / 211 (0.47%)
occurrences (all)	5	4	1
Blood urea increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Body temperature increased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Cardiac murmur			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	3
Colonoscopy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Crystal urine present			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram T wave abnormal			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram abnormal			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Electroencephalogram			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Eosinophil count increased			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2

Grip strength decreased			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Haemoglobin increased			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
High density lipoprotein decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Liver function test abnormal			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Low density lipoprotein increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Monocyte count decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
N-telopeptide urine increased			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	4	4	0
Neutrophil count decreased			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Neutrophil count increased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	2	1
Osteocalcin increased			
subjects affected / exposed	2 / 226 (0.88%)	3 / 216 (1.39%)	1 / 211 (0.47%)
occurrences (all)	4	6	2
Platelet count decreased			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0

Platelet count increased			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
QRS axis abnormal			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Red blood cells urine positive			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Thyroid function test abnormal			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Thyroxine decreased			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	3 / 211 (1.42%)
occurrences (all)	6	2	5
Thyroxine free decreased			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	3 / 211 (1.42%)
occurrences (all)	1	6	6
Thyroxine free increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Thyroxine increased			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	0	1	2
Tri-iodothyronine decreased			
subjects affected / exposed	3 / 226 (1.33%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	13	0	0
Tri-iodothyronine free decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	2	0	3
Tri-iodothyronine free increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0

Tri-iodothyronine increased			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Urinary sediment present			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Urine analysis abnormal			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Vitamin D decreased			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	2	1
Vitamin D increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	6 / 211 (2.84%)
occurrences (all)	2	1	8
Weight increased			
subjects affected / exposed	7 / 226 (3.10%)	7 / 216 (3.24%)	5 / 211 (2.37%)
occurrences (all)	12	12	7
White blood cell count decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	1	0	2
White blood cell count increased			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	0	4	1
White blood cells urine positive			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Accidental overdose			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	2	0	1
Animal bite			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	2	4	1
Arthropod sting			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Avulsion fracture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Back injury			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Burns first degree			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Burns second degree			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	2	0	1
Clavicle fracture			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Concussion			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	4	1	0
Contusion			
subjects affected / exposed	8 / 226 (3.54%)	6 / 216 (2.78%)	7 / 211 (3.32%)
occurrences (all)	16	10	8
Drug dose omission			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Drug toxicity			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Excoriation			
subjects affected / exposed	4 / 226 (1.77%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	6	5	5
Eye injury			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	3
Eyelid injury			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	1	0	3
Face injury			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Facial bones fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Fall			
subjects affected / exposed	11 / 226 (4.87%)	8 / 216 (3.70%)	5 / 211 (2.37%)
occurrences (all)	18	15	5
Fibula fracture			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Foot fracture			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	2	2	0
Forearm fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Fracture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Hand fracture			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	2	1
Head injury			

subjects affected / exposed	7 / 226 (3.10%)	5 / 216 (2.31%)	6 / 211 (2.84%)
occurrences (all)	12	8	11
Incision site pain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Injury			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Intentional overdose			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Jaw fracture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Joint dislocation			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Joint injury			
subjects affected / exposed	5 / 226 (2.21%)	7 / 216 (3.24%)	1 / 211 (0.47%)
occurrences (all)	7	7	1
Joint sprain			
subjects affected / exposed	2 / 226 (0.88%)	3 / 216 (1.39%)	3 / 211 (1.42%)
occurrences (all)	2	4	4
Laceration			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	6	1
Ligament injury			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Ligament rupture			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Ligament sprain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Limb injury			

subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	3 / 211 (1.42%)
occurrences (all)	3	1	4
Lip injury			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Multiple injuries			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Open wound			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Overdose			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Periorbital haematoma			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Post procedural complication			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Post procedural swelling			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Post-traumatic pain			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Procedural pain			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	2	3	0
Radius fracture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Rib fracture			

subjects affected / exposed	3 / 226 (1.33%)	3 / 216 (1.39%)	0 / 211 (0.00%)
occurrences (all)	4	3	0
Road traffic accident			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Scratch			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Skeletal injury			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	8 / 226 (3.54%)	8 / 216 (3.70%)	4 / 211 (1.90%)
occurrences (all)	12	11	4
Skull fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Spinal compression fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Subcutaneous haematoma			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Thermal burn			
subjects affected / exposed	5 / 226 (2.21%)	6 / 216 (2.78%)	3 / 211 (1.42%)
occurrences (all)	6	7	3
Thoracic vertebral fracture			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Tongue injury			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Tooth fracture			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	0	3	2
Traumatic brain injury			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	2	0	1
Traumatic haematoma			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Wrist fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	2	1
Atrioventricular block second degree			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Cardiac arrest			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Conduction disorder			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Dilatation ventricular			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Palpitations			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Right ventricular hypertrophy			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	1 / 226 (0.44%)	4 / 216 (1.85%)	2 / 211 (0.95%)
occurrences (all)	1	6	4
Tachycardia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	1	0	2

Ventricular extrasystoles			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	3 / 226 (1.33%)	6 / 216 (2.78%)	3 / 211 (1.42%)
occurrences (all)	5	8	4
Aphasia			
subjects affected / exposed	0 / 226 (0.00%)	3 / 216 (1.39%)	1 / 211 (0.47%)
occurrences (all)	0	3	2
Ataxia			
subjects affected / exposed	4 / 226 (1.77%)	10 / 216 (4.63%)	11 / 211 (5.21%)
occurrences (all)	4	16	16
Balance disorder			
subjects affected / exposed	4 / 226 (1.77%)	8 / 216 (3.70%)	8 / 211 (3.79%)
occurrences (all)	5	12	14
Basal ganglia infarction			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Burning sensation			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Carotid arteriosclerosis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Carpal tunnel syndrome			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	4	3	0
Cerebellar syndrome			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	6	1	2
Cervicobrachial syndrome			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Cognitive disorder			

subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	2 / 211 (0.95%)
occurrences (all)	5	3	2
Coordination abnormal			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	4 / 211 (1.90%)
occurrences (all)	0	2	4
Crying			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Decreased vibratory sense			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Disturbance in attention			
subjects affected / exposed	5 / 226 (2.21%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	8	2	2
Dizziness			
subjects affected / exposed	62 / 226 (27.43%)	60 / 216 (27.78%)	67 / 211 (31.75%)
occurrences (all)	110	114	122
Dizziness postural			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Drooling			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Dysarthria			
subjects affected / exposed	0 / 226 (0.00%)	3 / 216 (1.39%)	8 / 211 (3.79%)
occurrences (all)	0	5	9
Dysgeusia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Dysgraphia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Dyskinesia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	2
Grand mal convulsion			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Head discomfort			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	4
Headache			
subjects affected / exposed	45 / 226 (19.91%)	37 / 216 (17.13%)	50 / 211 (23.70%)
occurrences (all)	74	73	87
Hemianopia homonymous			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Hemicephalalgia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Hypersomnia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	0	1	3
Hypoaesthesia			
subjects affected / exposed	3 / 226 (1.33%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	4	6	2
Intention tremor			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Lethargy			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	3 / 211 (1.42%)
occurrences (all)	2	1	3
Loss of consciousness			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	1	3	1
Lumbar radiculopathy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Memory impairment			

subjects affected / exposed	5 / 226 (2.21%)	3 / 216 (1.39%)	6 / 211 (2.84%)
occurrences (all)	8	3	9
Migraine			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	3 / 211 (1.42%)
occurrences (all)	16	1	6
Monoparesis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Motor dysfunction			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Myoclonus			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Nerve compression			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Nystagmus			
subjects affected / exposed	2 / 226 (0.88%)	3 / 216 (1.39%)	5 / 211 (2.37%)
occurrences (all)	3	5	6
Paraesthesia			
subjects affected / exposed	3 / 226 (1.33%)	2 / 216 (0.93%)	6 / 211 (2.84%)
occurrences (all)	4	3	9
Partial seizures			
subjects affected / exposed	20 / 226 (8.85%)	10 / 216 (4.63%)	12 / 211 (5.69%)
occurrences (all)	21	16	15
Partial seizures with secondary generalisation			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	1	3	0
Peripheral nerve lesion			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0

Petit mal epilepsy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Postictal headache			
subjects affected / exposed	1 / 226 (0.44%)	3 / 216 (1.39%)	3 / 211 (1.42%)
occurrences (all)	1	6	3
Presyncope			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Psychomotor hyperactivity			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	2	0	1
Restless legs syndrome			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Sciatica			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	5	0	0
Sedation			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	1	2	3
Simple partial seizures			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Sinus headache			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	35 / 226 (15.49%)	30 / 216 (13.89%)	44 / 211 (20.85%)
occurrences (all)	50	43	66
Speech disorder			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	3	1
Status epilepticus			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0

Syncope			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	3 / 211 (1.42%)
occurrences (all)	0	1	3
Tension headache			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	2	0	1
Tongue biting			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Toxic encephalopathy			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	10 / 226 (4.42%)	10 / 216 (4.63%)	12 / 211 (5.69%)
occurrences (all)	14	13	21
Tunnel vision			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Visual field defect			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	4	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 226 (2.21%)	4 / 216 (1.85%)	3 / 211 (1.42%)
occurrences (all)	8	4	4
Eosinophilia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Granulocytopenia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Leukocytosis			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Lymphadenitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Lymphocytosis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Lymphopenia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Macrocytosis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Pancytopenia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Polycythaemia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Splenomegaly			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	0	1	2
Deafness bilateral			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Deafness neurosensory			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0

Deafness unilateral			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Ear pain			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Hearing impaired			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Mastoid disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Motion sickness			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Tinnitus			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	1	1	3
Vertigo			
subjects affected / exposed	15 / 226 (6.64%)	8 / 216 (3.70%)	18 / 211 (8.53%)
occurrences (all)	23	14	30
Vertigo positional			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Vestibular disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Blepharitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Cataract			

subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	3	4	0
Conjunctival ulcer			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 226 (0.00%)	4 / 216 (1.85%)	2 / 211 (0.95%)
occurrences (all)	0	5	2
Conjunctivitis allergic			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Diplopia			
subjects affected / exposed	17 / 226 (7.52%)	26 / 216 (12.04%)	28 / 211 (13.27%)
occurrences (all)	23	64	51
Dry eye			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Episcleritis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Eye irritation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	2
Eye pruritus			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	2	1	1
Eye swelling			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Eyelid oedema			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Glaucoma			

subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Keratitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Macular degeneration			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Metamorphopsia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Mydriasis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Ocular discomfort			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Oscillopsia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Panophthalmitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Pterygium			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Vision blurred			
subjects affected / exposed	9 / 226 (3.98%)	16 / 216 (7.41%)	13 / 211 (6.16%)
occurrences (all)	10	26	19
Visual acuity reduced			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	1	2	2
Visual impairment			

subjects affected / exposed	4 / 226 (1.77%)	4 / 216 (1.85%)	1 / 211 (0.47%)
occurrences (all)	5	5	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 226 (0.00%)	3 / 216 (1.39%)	3 / 211 (1.42%)
occurrences (all)	0	5	4
Abdominal distension			
subjects affected / exposed	1 / 226 (0.44%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	1	3	2
Abdominal pain			
subjects affected / exposed	7 / 226 (3.10%)	4 / 216 (1.85%)	6 / 211 (2.84%)
occurrences (all)	9	10	8
Abdominal pain upper			
subjects affected / exposed	8 / 226 (3.54%)	5 / 216 (2.31%)	6 / 211 (2.84%)
occurrences (all)	11	7	6
Anal fissure			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Colitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Colonic polyp			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	11 / 226 (4.87%)	10 / 216 (4.63%)	11 / 211 (5.21%)
occurrences (all)	14	12	15
Defaecation urgency			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Dental caries			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Diarrhoea			
subjects affected / exposed	15 / 226 (6.64%)	14 / 216 (6.48%)	8 / 211 (3.79%)
occurrences (all)	22	24	11

Dry mouth			
subjects affected / exposed	2 / 226 (0.88%)	3 / 216 (1.39%)	5 / 211 (2.37%)
occurrences (all)	3	5	6
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	8 / 226 (3.54%)	3 / 216 (1.39%)	6 / 211 (2.84%)
occurrences (all)	14	5	8
Enteritis			
subjects affected / exposed	3 / 226 (1.33%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Flatulence			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Frequent bowel movements			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	6 / 226 (2.65%)	5 / 216 (2.31%)	2 / 211 (0.95%)
occurrences (all)	7	8	3
Gastrointestinal pain			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 226 (0.88%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	2	6	3
Gingival hyperplasia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Gingivitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0

Glossodynia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	2	3	1
Hypoaesthesia oral			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	2	2	2
Infrequent bowel movements			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	2	1
Inguinal hernia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Intestinal polyp			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Loose tooth			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Mouth ulceration			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	25 / 226 (11.06%)	31 / 216 (14.35%)	39 / 211 (18.48%)
occurrences (all)	31	41	51
Odynophagia			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0

Oesophagitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Oral dysaesthesia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Pancreatic atrophy			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Paraesthesia oral			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	2
Periodontal disease			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Periodontitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Retching			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Salivary gland calculus			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Sensitivity of teeth			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Tongue ulceration			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0

Tooth disorder			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Tooth loss			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Toothache			
subjects affected / exposed	7 / 226 (3.10%)	4 / 216 (1.85%)	8 / 211 (3.79%)
occurrences (all)	9	5	8
Umbilical hernia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	14 / 226 (6.19%)	16 / 216 (7.41%)	29 / 211 (13.74%)
occurrences (all)	19	28	37
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Liver disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	1	4	3
Alopecia			
subjects affected / exposed	2 / 226 (0.88%)	4 / 216 (1.85%)	1 / 211 (0.47%)
occurrences (all)	3	5	1
Blister			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Chloasma			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Dandruff			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Dermatitis atopic			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	4	0
Dermatitis contact			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	1	1	2
Drug eruption			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Ecchymosis			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	2	3	1
Eczema			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	2
Erythema			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Hair texture abnormal			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Heat rash			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			

subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	2	2	0
Hypertrophic scar			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Hypoaesthesia facial			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Increased tendency to bruise			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Ingrowing nail			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Macule			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Polymorphic light eruption			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Pruritus			
subjects affected / exposed	5 / 226 (2.21%)	2 / 216 (0.93%)	5 / 211 (2.37%)
occurrences (all)	6	3	7
Pruritus generalised			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	6 / 226 (2.65%)	5 / 216 (2.31%)	8 / 211 (3.79%)
occurrences (all)	10	7	8
Rash erythematous			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Rash generalised			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Rash papular			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Rash pruritic			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Rash vesicular			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Scab			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Scar			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Seborrhoea			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Skin disorder			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Skin exfoliation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Skin ulcer			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Swelling face			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Urticaria			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Chromaturia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Haematuria			
subjects affected / exposed	4 / 226 (1.77%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	6	0	1
Hypertonic bladder			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	3	0	2
Micturition urgency			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Nephrolithiasis			
subjects affected / exposed	5 / 226 (2.21%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	8	2	4
Nocturia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	3 / 226 (1.33%)	2 / 216 (0.93%)	1 / 211 (0.47%)
occurrences (all)	4	4	2
Renal colic			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0

Renal failure			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	3	0	1
Renal failure acute			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Urethral pain			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Urinary hesitation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Goitre			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Hyperthyroidism			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Hypogonadism			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	7 / 226 (3.10%)	9 / 216 (4.17%)	5 / 211 (2.37%)
occurrences (all)	10	16	11
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 226 (2.65%)	5 / 216 (2.31%)	2 / 211 (0.95%)
occurrences (all)	12	9	2
Axillary mass			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Back pain			
subjects affected / exposed	14 / 226 (6.19%)	13 / 216 (6.02%)	5 / 211 (2.37%)
occurrences (all)	22	24	6
Bone metabolism disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	3 / 211 (1.42%)
occurrences (all)	0	0	5
Bone pain			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Bursitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Cervical spinal stenosis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Coccydynia			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Finger deformity			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Groin pain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Intervertebral disc degeneration			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	0	1	3
Intervertebral disc protrusion			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	3	1	2
Joint contracture			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Joint instability			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	4 / 226 (1.77%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	6	1	1
Muscular weakness			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	2 / 211 (0.95%)
occurrences (all)	4	4	3
Musculoskeletal chest pain			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	2	1
Musculoskeletal discomfort			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	2	1
Musculoskeletal pain			
subjects affected / exposed	9 / 226 (3.98%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	19	3	2
Musculoskeletal stiffness			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	5 / 226 (2.21%)	6 / 216 (2.78%)	5 / 211 (2.37%)
occurrences (all)	8	12	9
Myokymia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	8 / 211 (3.79%)
occurrences (all)	2	1	10
Osteoarthritis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Osteomalacia			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Osteonecrosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Osteopenia			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Osteoporosis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	8 / 226 (3.54%)	6 / 216 (2.78%)	3 / 211 (1.42%)
occurrences (all)	16	12	3
Pain in jaw			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Periarthritis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Posture abnormal			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Sjogren's syndrome			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	2	2
Systemic lupus erythematosus			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Tendon pain			

subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Tendonitis			
subjects affected / exposed	3 / 226 (1.33%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	4	0	3
Tenosynovitis stenosans			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Trigger finger			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Acute sinusitis			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Acute tonsillitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Bacterial infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Bacteriuria			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Bronchitis			
subjects affected / exposed	6 / 226 (2.65%)	4 / 216 (1.85%)	2 / 211 (0.95%)
occurrences (all)	7	5	2
Candidiasis			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0

Cellulitis			
subjects affected / exposed	2 / 226 (0.88%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	3	2	0
Cystitis			
subjects affected / exposed	0 / 226 (0.00%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Ear infection			
subjects affected / exposed	3 / 226 (1.33%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	6	0	0
Erysipelas			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Eye infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	2
Fungal infection			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Furuncle			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	4	1	1
Gastroenteritis viral			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Genital infection female			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Gingival abscess			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1

Gingival infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Hepatitis C			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	3	0
Herpes zoster			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	1	2	0
Hordeolum			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	1	0	1
Infection			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	12 / 226 (5.31%)	10 / 216 (4.63%)	9 / 211 (4.27%)
occurrences (all)	16	11	11
Labyrinthitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Nail infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	25 / 226 (11.06%)	21 / 216 (9.72%)	13 / 211 (6.16%)
occurrences (all)	38	31	19

Onychomycosis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Otitis externa			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Papilloma viral infection			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Pharyngitis			
subjects affected / exposed	9 / 226 (3.98%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	16	2	0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	1	1	3
Postoperative wound infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Pulpitis dental			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Pyelonephritis chronic			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	3	1	2

Respiratory tract infection viral			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	2 / 211 (0.95%)
occurrences (all)	0	1	2
Rhinitis			
subjects affected / exposed	5 / 226 (2.21%)	4 / 216 (1.85%)	0 / 211 (0.00%)
occurrences (all)	5	6	0
Sepsis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	4 / 226 (1.77%)	2 / 216 (0.93%)	3 / 211 (1.42%)
occurrences (all)	5	2	4
Skin infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Staphylococcal infection			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Tinea cruris			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Tinea infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Tinea pedis			
subjects affected / exposed	1 / 226 (0.44%)	2 / 216 (0.93%)	0 / 211 (0.00%)
occurrences (all)	3	4	0
Tonsillitis			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	3	1	1
Tonsillitis bacterial			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	2 / 211 (0.95%)
occurrences (all)	0	0	2

Upper respiratory tract infection			
subjects affected / exposed	9 / 226 (3.98%)	10 / 216 (4.63%)	8 / 211 (3.79%)
occurrences (all)	13	17	8
Urethritis trichomonal			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	10 / 226 (4.42%)	14 / 216 (6.48%)	6 / 211 (2.84%)
occurrences (all)	14	18	9
Vaginal infection			
subjects affected / exposed	3 / 226 (1.33%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	3	2	0
Vaginitis bacterial			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	4 / 226 (1.77%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	4	0	0
Viral sinusitis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 226 (4.42%)	7 / 216 (3.24%)	8 / 211 (3.79%)
occurrences (all)	13	10	10
Dehydration			
subjects affected / exposed	1 / 226 (0.44%)	3 / 216 (1.39%)	2 / 211 (0.95%)
occurrences (all)	1	3	2
Diabetes mellitus			

subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	3	0	0
Dyslipidaemia			
subjects affected / exposed	2 / 226 (0.88%)	6 / 216 (2.78%)	7 / 211 (3.32%)
occurrences (all)	3	9	13
Food craving			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	2	0
Gout			
subjects affected / exposed	0 / 226 (0.00%)	0 / 216 (0.00%)	1 / 211 (0.47%)
occurrences (all)	0	0	1
Hypercholesterolaemia			
subjects affected / exposed	5 / 226 (2.21%)	2 / 216 (0.93%)	3 / 211 (1.42%)
occurrences (all)	10	4	5
Hyperglycaemia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	1	1	0
Hyperlipidaemia			
subjects affected / exposed	2 / 226 (0.88%)	0 / 216 (0.00%)	3 / 211 (1.42%)
occurrences (all)	3	0	6
Hypertriglyceridaemia			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	2	1	0
Hypochloraemia			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Hypoglycaemia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	1 / 226 (0.44%)	3 / 216 (1.39%)	1 / 211 (0.47%)
occurrences (all)	1	3	2
Hyponatraemia			

subjects affected / exposed	7 / 226 (3.10%)	8 / 216 (3.70%)	10 / 211 (4.74%)
occurrences (all)	7	11	11
Hypophagia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Increased appetite			
subjects affected / exposed	2 / 226 (0.88%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	3	1	0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 226 (0.44%)	0 / 216 (0.00%)	0 / 211 (0.00%)
occurrences (all)	2	0	0
Vitamin B12 deficiency			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	1 / 211 (0.47%)
occurrences (all)	1	1	1
Vitamin D deficiency			
subjects affected / exposed	1 / 226 (0.44%)	1 / 216 (0.46%)	3 / 211 (1.42%)
occurrences (all)	2	4	3
Weight loss poor			
subjects affected / exposed	0 / 226 (0.00%)	1 / 216 (0.46%)	0 / 211 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 April 2009	Global Protocol Amendment #1: Reason for amendment: The following parts are adapted/changed: -Inclusion Criteria -Exclusion Criteria -Volume of Blood Samples -Adverse Events -Serious Adverse Events -Pregnancies -Special cases reporting -Withdrawal Criteria -Number of Study Sites -Patient Treatment Unblinding -Laboratory tests -Introduction -Taper off strategy -First intake of medication -Warnings -Scales and questionnaires -Data collection, verification and coding -Update of Investigator Brochure -Country specific changes will be implemented as country specific protocol amendments in countries with existing country specific protocol amendments (Germany and Argentina). -Contact Details Medical Monitor changed
01 December 2009	Global Protocol Amendment #2: Reason for amendment: 1. A Sponsor for North America is introduced and additional personnel details included. "The Sponsor" now refers to either BIAL (Europe and South America) or Sepracor (North America). 2. The United States (US) and Canada are included in the list of participating countries and the number of sites increased. 3. The drug code used by the North America Sponsor is added. 4. The dosing schedule diagram is clarified. 5. Contact by telephone is added between V5 and V6. 6. The primary and secondary efficacy analyses are clarified as "change of seizure frequency" rather than "seizure frequency". 7. In the inclusion criteria, a requirement for patients aged 16 to 18 years in North America to sign an assent is added. 8. Stratification by region (North America versus Europe and South America) is introduced in Section 5 and Section 11.2.2 is amended accordingly. 9. Section 6 is divided so that drug formulation, labelling, storage and packaging information specific to North America is included in addition to specific information for Europe and South America. 10. A fax number in the US for reporting SAEs occurring in North America is added in Section 10.7. 11. New details on objective findings are added in Section 10.9. 12. Details relating to financial disclosure are added in Section 12.2. 13. Information on computerised systems used in the US is included in Section 12.6 and Appendix I. 14. North America-specific information on patient confidentiality is added in Section 13.9. 15. Independent Ethics Committee (IEC) is amended to IEC/Institutional Review Board (IRB) throughout the protocol.

16 September 2010	"Global Protocol Amendment #3: Reason for amendment: 1. Updated guidelines for titration steps for Part III 2. Vagus nerve stimulation is not counted as anti-epileptic drug 3. Serum sodium <125 mmol/L was included as a withdrawal criterion 4. Clarification for exclusion criteria for history of schizophrenia 5. Added an option to reduce the dose of concomitant carbamazepine 6. Screening for presence of HLA-B*1502 allele in patients of Asian ancestry is exclusion criterion 7. Number of patients to be enrolled and number of sites and countries updated 8. Exclusion criteria participation in previous Eslicarbazepine acetate trials or other clinical trials is modified 9. Change in Pharmanet and Bial/Sepracor study personnel information 10. Updated wording for primary and secondary endpoints 11. Seizure diary adapted to require diary entries every day, regardless of whether a seizure had occurred 12. Changed the procedure for collecting seizure data from the diaries 13. Increased sample size 14. Updated definition of analysis populations 15. Provided specificity on definition of baseline and maintenance periods 16. Updated wording of efficacy endpoints 17. Updated statistical methodology 18. Separate analyses for patients who used Event Entry diaries and Daily Entry diaries will be performed 19. Added Columbia Suicide Severity Rating Scale assessment throughout the protocol 20. Added post-treatment assessment of withdrawal symptoms, adverse events and seizure worsening 21. Added telephone contact 3 to occur approximately 3 weeks prior to Post-study visit 22. Clarification regarding randomization patients with at least 3 partial-onset seizures in a 4-week section of the baseline period 23. Patients must have no seizure-free interval exceeding 28 consecutive days during the baseline period
15 February 2011	Global Protocol Amendment #4 Reason for amendment - Additional 2-year open-label extension (Part III) - Changes in footnotes - Added text that in Discontinuation visit/EDV dispensing of investigational product will occur for patients performing down titration only - Revised ROW Safety contact at CRO - Additional secondary objective added - Changes in maximum number of patients allowed to be recruited per site - Corrected spelling of the word preceded. - Adaption in Study Flow Chart - Inclusion criterion 7 adapted - Criterion 11 corrected - Part III to section patient enrolment and randomisation added - Clarification that “dispensed” bottles will contain sufficient Eslicarbazepine acetate tablets for the subsequent period before next visit plus 2 extra weeks. - Addition of text for rescue medication. - Clarification that seizure diaries will be kept only for Part I and Part II of the study. - Clarification when CGI ratings will be performed - Clarification that the CSSRS scale will be administered by the study personnel - Added medication accountability to Post-Study visit. - Revision of Edition and date of Bial’s Investigator’s Brochure information - Revision of Edition and date of Sepracor’s Investigator’s Brochure information - Update of name and webadress due to namechange of Sepracor Inc. - Revised telephone number for Pharmanet Project manager - Information of collected data in Part III and planned analysis updatedalysis of CGI, retention rates and AEs and that other analysis might be planned.

28 July 2011	Global Protocol Amendment #5 Reason for amendment - Modifications in section Study Drug Dosage, Administration and Schedule - Clarification of section Previous and Concomitant Therapy and Rescue Medication - Complement to section Previous and Concomitant Therapy and Rescue Medication - Complement to section Study Procedures for Safety and Efficacy Evaluations - Complement to section Evaluations and Procedures by Visit - Changes in section Criteria for Patient Withdrawal - Changes in section for Serious Adverse Events - Complement to section Statistical Methods - Changes in section Administrative revisions - Minor copy revisions to ensure proper format and consistency

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported