Clinical trial results:
A 12-MONTH OPEN-LABEL EXTENSION STUDY EVALUATING THE SAFETY AND TOLERABILITY OF FLEXIBLE DOSES OF PREGABALIN IN PEDIATRIC PATIENTS WITH PARTIAL ONSET SEIZURES

Summary

EudraCT number	2010-020731-39
Trial protocol	FR
Global end of trial date	09 October 2013

Results information

Result version number	v1 (current)
This version publication date	30 May 2016
First version publication date	23 July 2015

Trial information

Trial identification

Sponsor protocol code	A0081075

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00448916
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 1-800 718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 1-800 718-1021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 February 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 October 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of pregabalin in pediatric subjects 1 month through 16 years of age with partial onset seizures.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed; in particular, those affording greater protection to the safety of study subjects.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	13 May 2007
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	Korea, Republic of: 3
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	United States: 47
Worldwide total number of subjects	54
EEA total number of subjects	0

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)	16
Children (2-11 years)	27
Adolescents (12-17 years)	11
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was a dose extension study of pediatric subjects with refractory partial-onset seizures who had completed study A0081074 (NCT00437281, Eudra CT number 2010-020730-26). Subjects were enrolled in 3 countries at 13 study centers with 13 investigators: Republic of Korea (1 center), Mexico (1 center), and the United States (11 centers).

Pre-assignment

Screening details:

Each subject was restricted to the dose levels that they had previously tolerated, or that had shown acceptable safety and tolerability in study A0081074 (NCT00437281, Eudra CT number 2010-020730-26) for the subject's age group.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Pregabalin: 1-23 Months

Arm description:

Age group included 1-23 months. Pregabalin was administered for 12 Months.

Arm type	Experimental
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	
Other name	Lyrica
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Pregabalin was administered orally as liquid formulation at dose of 2.5, 5, 7.5, 10, or 15 milligram per kilogram per day (mg/kg/day) for 12 Months.

Arm title	Pregabalin: 2-6 Years

Arm description:

Age group included 2-6 years. Pregabalin was administered for 12 Months.

Arm type	Experimental
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	
Other name	Lyrica
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Pregabalin was administered orally as liquid formulation at dose of 2.5, 5, 7.5, 10, or 15 mg/kg/day for 12 Months.

Arm title	Pregabalin: 7-11 Years

Arm description:

Age group included 7-11 years. Pregabalin was administered for 12 Months.

Arm type	Experimental

Investigational medicinal product name	Pregabalin
Investigational medicinal product code	
Other name	Lyrica
Pharmaceutical forms	Capsule, Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Pregabalin was administered orally as capsule formulation or liquid formulation. Doses of 2.5, 5, 7.5, 10, or 15 mg/kg/day were given for 12 Months.

Arm title	Pregabalin: 12-16 Years

Arm description:

Age group included 12-16 years. Pregabalin was administered for 12 Months.

Arm type	Experimental
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	
Other name	Lyrica
Pharmaceutical forms	Capsule, Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Pregabalin was administered orally as capsule formulation or liquid formulation. Doses of 2.5, 5, 7.5, 10, or 15 mg/kg/day were given for 12 Months.

Number of subjects in period 1	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years
Started	16	15	12
Completed	9	9	6
Not completed	7	6	6
Consent withdrawn by subject	3	3	1
Adverse Event	2	2	3
Not specified	1	-	-
Protocol Violation	-	-	-
Lost to follow-up	-	1	-
Lack of efficacy	1	-	2

Number of subjects in period 1	Pregabalin: 12-16 Years
Started	11
Completed	5
Not completed	6
Consent withdrawn by subject	1
Adverse Event	2
Not specified	-
Protocol Violation	1
Lost to follow-up	1
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Pregabalin: 1-23 Months
Reporting group description:	
Age group included 1-23 months. Pregabalin was administered for 12 Months.	

Reporting group title	Pregabalin: 2-6 Years
Reporting group description:	
Age group included 2-6 years. Pregabalin was administered for 12 Months.	
Reporting group title	Pregabalin: 7-11 Years
Reporting group description:	
Age group included 7-11 years. Pregabalin was administered for 12 Months.	
Reporting group title	Pregabalin: 12-16 Years
Reporting group description:	
Age group included 12-16 years. Pregabalin was administered for 12 Months.	

Reporting group values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years
Number of subjects	16	15	12
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	1.18	4.14	9.98
standard deviation	± 0.57	± 1.23	± 1.3
Gender categorical Units: Subjects			
Female	8	9	5
Male	8	6	7

Reporting group values	Pregabalin: 12-16 Years	Total	
Number of subjects	11	54	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	14.86		
standard deviation	± 1.53	-	
Gender categorical Units: Subjects			
Female	3	25	
Male	8	29	

End points

End points reporting groups

Reporting group title	Pregabalin: 1-23 Months
Reporting group description:	
Age group included 1-23 months. Pregabalin was administered for 12 Months.	

Reporting group title	Pregabalin: 2-6 Years
Reporting group description:	
Age group included 2-6 years. Pregabalin was administered for 12 Months.	

Reporting group title	Pregabalin: 7-11 Years
Reporting group description:	
Age group included 7-11 years. Pregabalin was administered for 12 Months.	

Reporting group title	Pregabalin: 12-16 Years
Reporting group description:	
Age group included 12-16 years. Pregabalin was administered for 12 Months.	

Primary: Number of Subjects With Adverse Events (AE)

End point title	Number of Subjects With Adverse Events (AE)[1]
End point description:	
An AE is any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. A serious adverse event (SAE) is any untoward medical occurrence at any dose that: results in death; is life-threatening (immediate risk of death); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; results in congenital anomaly/birth defect. Safety analysis set: All subjects who received at least one dose of study medication were included.	
End point type	Primary
End point timeframe:	
12 Months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be reported for this endpoint.

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
Subjects with AEs	14	13	11	9
Subjects with serious AEs	8	3	0	1
Subjects with severe AEs	7	4	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Change From Previous Physical Examination Results at Visit 1, Week 1, Month 1, Month 6, Month 12/Early Termination and Follow-up

End point title	Number of Subjects With Change From Previous Physical Examination Results at Visit 1, Week 1, Month 1, Month 6, Month 12/Early Termination and Follow-up

End point description:

Changes from previous examinations in physical examination were reported. Examination of abdomen, breasts, ears, extremities, eyes, genitourinary, head, heart, lungs, lymph nodes, mouth, musculoskeletal, neck, nose, ocular fundi, skin, throat, thyroid and general examinations were done. Evaluation was done based on presence of abnormality which were noted as "abnormal" and no abnormalities in the sites were reported as "normal". Any change from the previous physical examination results were noted. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

Visit 1, Week 1, Month 1, Month 6, Month 12/Early Termination and Follow-up.

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
Week 1 (N=16,13,11,10)	2	1	0	0
Month 1 (N=14,13,10,10)	1	1	0	0
Month 6 (N=11,10,6,7)	1	1	0	0
Month 12/Early Termination (N=16,12,12,9)	1	2	1	1
Follow-up (N=6,4,9,6)	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Change From Previous Neurological Examination Results at Visit 1, Week 1, Month 1, Month 6, Month 12/Early Termination and Follow-up

End point title	Number of Subjects With Change From Previous Neurological Examination Results at Visit 1, Week 1, Month 1, Month 6, Month 12/Early Termination and Follow-up

End point description:

Changes from previous examinations in neurological examination were reported. The neurologic exam were performed by a pediatric neurologist or qualified staff member. Coordination, cranial nerves, gait, level of consciousness, lower and upper extremity sensation, muscle strength, muscle tone, nystagmus, reflexes, Romberg test, and speech were examined. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

Visit 1, Week 1, Month 1, Month 6, Month 12/Early Termination and Follow-up

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
Week 1 (N=16,13,11,10)	1	0	0	0
Month 1 (N=14,13,10,10)	0	0	0	0
Month 6 (N=11,10,6,7)	0	0	0	0
Month 12/Early Termination (N=16,11,12,9)	0	0	0	0
Follow-up (N=6,4,9,6)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Significant Change in Supine Diastolic Blood Pressure (BP) at Post-Baseline Visits (Visit 1 to 12 Months)

End point title	Number of Subjects With Significant Change in Supine Diastolic Blood Pressure (BP) at Post-Baseline Visits (Visit 1 to 12 Months)

End point description:

Subjects with significant supine diastolic BP values with the criteria greater than or equal to (≥)20 percent (%) increase from Baseline or ≥20% decrease from Baseline or greater than (>)1.25 times upper limit of normal (ULN) or less than (<)0.9 times lower limit of normal (LLN) were identified and recorded. The categorical summary of Post-Baseline supine diastolic BP data are presented below. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

Visit 1 to 12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
≥ 20% increase from Baseline	12	5	8	3
≥ 20% decrease from Baseline	5	7	3	3
> 1.25 * ULN	1	1	0	0
< 0.9 * LLN	0	0	3	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Significant Change in Supine Systolic BP at Post Baseline Visits (Visit 1 to 12 Months)

End point title	Number of Subjects With Significant Change in Supine Systolic BP at Post Baseline Visits (Visit 1 to 12 Months)

End point description:

Subjects with significant supine systolic BP values with the criteria ≥30% increase from Baseline or ≥30% decrease from Baseline or >1.25 times ULN or <0.9 times LLN were identified and recorded. The categorical summary of Post-Baseline supine systolic BP data are presented below. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

Visit 1 to 12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
≥ 30% increase from Baseline	2	3	1	1
≥ 30% decrease from Baseline	2	1	0	0
> 1.25 * ULN	0	0	0	0
< 0.9 * LLN	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Significant Change in Supine Heart Rate (HR) at Post Baseline Visits (Visit 1 to 12 Months)

End point title	Number of Subjects With Significant Change in Supine Heart Rate (HR) at Post Baseline Visits (Visit 1 to 12 Months)

End point description:

Subjects with significant heart rate values with the criteria > 1.5 times ULN or < 0.9 times LLN were identified and recorded. The categorical summary of Post-Baseline supine HR data are presented below. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:
Visit 1 to 12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
> 1.5 * ULN	0	0	0	0
< 0.9 * LLN	5	2	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Derived Body Mass Index Data (BMI) at Month 12/Early Termination

End point title	Derived Body Mass Index Data (BMI) at Month 12/Early Termination

End point description:

BMI was calculated from height and weight measured at Month 12 visit using the formula: weight(kg)/height (meter [m])^2. Safety analysis set: All subjects who received at least one dose of study medication were included. Data was available for 15, 11, 10 and 7 subjects in Pregabalin 1-23 months group, 2-6 years group, 7-11 years group and 12-16 years group respectively.

End point type	Secondary

End point timeframe:
Month 12/Early Termination

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	11	10	7
Units: Kg/m^2				
arithmetic mean (standard deviation)	16.2 (± 1.73)	18 (± 3.52)	20.6 (± 6.52)	24.8 (± 7.72)

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Body Weight at Day 9, Week 1, Month 1, Month 2, Month 4, Month 6, Month 9, Month 12/Early Termination and Follow-up

End point title	Change From Baseline in Body Weight at Day 9, Week 1, Month 1, Month 2, Month 4, Month 6, Month 9, Month 12/Early Termination and Follow-up

End point description:

Weight was recorded in kilograms and weight change from Baseline was reported. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

Baseline, Day 9, Week 1, Month 1, Month 2, Month 4, Month 6, Month 9, Month 12/Early Termination and Follow-up.

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: Kg				
arithmetic mean (standard deviation)				
Day 9 (N=16,14,12,11)	0.1 (± 0.16)	0.1 (± 0.29)	-0.1 (± 0.79)	0.4 (± 1.07)
Week 1 (N=16,13,11,10)	0.3 (± 0.29)	0.4 (± 0.61)	1.5 (± 1.15)	1.2 (± 1.43)
Month 1 (N=14,13,10,10)	0.4 (± 0.45)	0.8 (± 0.73)	2.1 (± 1.77)	2.4 (± 1.52)
Month 2 (N=11,12,8,9)	1 (± 0.73)	1.2 (± 1.12)	3.8 (± 3.25)	3 (± 1.81)
Month 4 (N=11,10,7,9)	1.3 (± 0.86)	1.3 (± 1.29)	5.2 (± 4.32)	4.1 (± 2.28)
Month 6 (N=11,10,6,7)	1.8 (± 0.98)	1.4 (± 1.52)	5.9 (± 4.17)	5.9 (± 3.32)
Month 9 (N=9,10,6,5)	2.4 (± 1.18)	2.3 (± 2.52)	6.3 (± 4.66)	7.3 (± 4.32)
Month 12/Early Termination (N=15,12,11,8)	1.8 (± 1.33)	2.4 (± 2.71)	6 (± 4.78)	6.6 (± 4.51)

Statistical analyses

No statistical analyses for this end point

Secondary: Height at Month 12/Early Termination

End point title	Height at Month 12/Early Termination

End point description:

Height was recorded in centimeters (cm). Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

Month 12/Early Termination

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	11	10	7
Units: cm				
arithmetic mean (standard deviation)	83.3 (± 8.87)	109.9 (± 12.76)	145.6 (± 13.21)	167.3 (± 8.18)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Changes in Electrocardiogram (ECG) Data Post-Baseline Visits (Week 1 to 12 Months)

End point title	Number of Subjects With Changes in Electrocardiogram (ECG) Data Post-Baseline Visits (Week 1 to 12 Months)

End point description:

Based on the criteria for safety values of potential clinical concern, the PR interval (≥200 millisecond (msec); ≥25% increase from Baseline; ≥50% increase from Baseline), QRS complex (≥200 msec; ≥25% increase from Baseline), QT interval (≥500 msec), maximum QTcB (QTc[Bazett's correction]) interval (450-<480; 480-<500; ≥500 msec) and maximum QTcF (QTc[Fridericia's correction]) interval (450-<480; 480-<500; ≥500 msec) values were calculated. Baseline was defined as Day 1 of the parent study A0081074 (NCT00437281). Categorical data of the Post-Baseline vists are represented below. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

Week 1 to 12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
PR interval: ≥ 200 msec	0	0	0	0
PR interval: ≥50% increase from Baseline	0	0	0	0
PR interval: ≥25% increase from Baseline	1	0	1	0
QRS interval: ≥ 200 msec	0	0	0	0
QRS interval: ≥25% increase from Baseline	0	0	0	0
QT interval: ≥ 500 msec	0	0	0	0
QTcB interval: 450-<480 msec	1	1	1	2
QTcB interval: 480-<500 msec	0	0	0	0
QTcB interval: ≥ 500 msec	0	0	0	0
QTcF interval: 450-<480 msec	0	0	0	0
QTcF interval: 480-<500 msec	0	0	0	0
QTcF interval: ≥ 500 msec	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Hematolgical Abnormalities

End point title	Number of Subjects With Hematolgical Abnormalities

End point description:

Based on criteria for safety values of potential clinical concern, the subjects with abnormal values were noted. Some of the values are: platelets (10*3/ millimeter[mm]*3): <0.5 LLN or >1.75 ULN; white blood cell (WBC) count (X10E9/L): <0.6 LLN or >1.5 ULN; lymphocytes-Absolute (Abs) (10*3/mm*3): <0.8 LLN or >1.2 ULN; total neutrophils-Abs (10*3/mm*3): <0.8 LLN or >1.2 ULN; and eosinophils-Abs: >1.2 ULN. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
Platelets: <0.5xLLN (N=16,15,12,11)	1	1	0	0
Platelets: >1.75xULN (N=16,15,12,11)	1	0	0	0
WBC count: <0.6xLLN (N=15,15,12,11)	1	2	0	0
WBC count: >1.5xULN (N=15,15,12,11)	0	0	0	0
Lymphocytes-Abs: <0.8xLLN (N=15,15,12,11)	0	0	0	0
Lymphocytes-Abs: >1.2xULN (N=15,15,12,11)	1	0	0	2
Total neutrophils-Abs: <0.8xLLN (N=15,15,12,11)	3	4	3	3
Total neutrophils-Abs: >1.2xULN (N=15,15,12,11)	1	1	0	0
Eosinophils-Abs: >1.2xULN (N=15,15,12,11)	3	1	1	0
Hemoglobin: <0.8xLLN(N=15,15,12,11)	0	0	0	0
Hematocrit: <0.8xLLN (N=15,15,12,11)	0	0	0	0
Red blood cell count: <0.8xLLN (N=15,15,12,11)	0	0	0	0
Basophils: >1.2xULN (N=15,15,12,11)	0	0	0	0
Monocytes: >1.2xULN (N=15,15,12,11)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Urinalysis (Dipstick/Microscopy)

End point title	Number of Subjects With Abnormalities in Urinalysis (Dipstick/Microscopy)

End point description:

Based on criteria for safety values of potential clinical concern, the subjects with abnormal values were noted. Subjects with Urine Protein milligram per deciliter (mg/dL) abnormalities (≥1) were noted based on urinalysis (dipstick). No subjects with abnormalities in urinalysis (microscopy) were noted. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	11	11
Units: subjects				
number (not applicable)	1	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Endocrine Panel (Hormones)

End point title	Number of Subjects With Abnormalities in Endocrine Panel (Hormones)

End point description:

Based on criteria for safety values of potential clinical concern, the subjects with abnormal values were noted. Some of the criteria are: Free thyroxine (T4 free) nanogram per deciliter (ng/dL): <0.8 LLN or >1.2 ULN and Thyroid-stimulating hormone (TSH) milliunits per liter (mu/L): <0.8 LLN or >1.2 ULN. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)				
T4 (free): <0.8xLLN (N=13,13,11,10)	0	1	0	0
T4 (free): >1.2xULN (N=13,13,11,10)	0	0	0	0
TSH: <0.8xLLN (N=14,12,11,10)	1	0	0	0
TSH: >1.2xULN (N=14,12,11,10)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Creatine Kinase

End point title	Number of Subjects With Abnormalities in Creatine Kinase

End point description:

Based on criteria for safety values of potential clinical concern, the subjects with abnormal values in creatine kinase (>2.0 times upper limit of the reference range) units per liter (u/L) were noted. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	12	11
Units: subjects				
number (not applicable)	0	1	1	4

Statistical analyses

No statistical analyses for this end point

Secondary: Seizure Frequency

End point title	Seizure Frequency

End point description:

Twenty-eight-day seizure frequencies were to be calculated from the seizure diaries and were to be reviewed. However, due to the nature of the data collection and due to inability to clearly differentiate no seizures versus seizures, accurate computation of this data was not performed. Hence, the seizure data was reported as AE. Safety analysis set: All subjects who received at least one dose of study medication were included. Here "99999" in the seizure frequency signifies not available (NA). Due to the nature of the data collection and due to inability to clearly differentiate no seizures versus seizures, accurate computation of this data was not performed.

End point type	Secondary

End point timeframe:

28 Days

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	12	11
Units: subjects				
number (not applicable)	99999	99999	99999	99999

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Abnormalities in Chemistry (Including Liver Function, Renal Function, Lipids, Electrolytes, Glucose, Insulin Like Growth Factor (IGF) and IGF Binding Protein)

End point title	Number of Subjects With Abnormalities in Chemistry (Including Liver Function, Renal Function, Lipids, Electrolytes, Glucose, Insulin Like Growth Factor (IGF) and IGF Binding Protein)

End point description:

Based on criteria for safety values of potential clinical concern, the subjects with abnormal values in liver function tests, renal function tests, lipid profile, electrolytes, glucose, Insulin like growth factor (IGF) and IGF binding protein were noted and reported in this section. Safety analysis set: All subjects who received at least one dose of study medication were included.

End point type	Secondary

End point timeframe:

12 Months

End point values	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years	Pregabalin: 12-16 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	15	12	11
Units: subjects				
number (not applicable)				
Alanine Aminotransferase: >3.0xULN (N=15,15,12,11)	0	1	1	0
Blood Urea Nitrogen: >1.3xULN	2	5	1	0
Albumin: <0.8xLLN (N=15,15,12,11)	0	0	0	0
Albumin: >1.2xULN (N=15,15,12,11)	2	0	0	0
Potassium: <0.9xLLN (N=15,15,12,11)	0	0	0	0
Potassium: >1.1xULN (N=15,15,12,11)	1	0	1	0
Magnesium: <0.9xLLN (N=15,15,12,11)	0	0	0	0
Magnesium: >1.1xULN (N=15,15,12,11)	1	2	0	1
Phosphate: <0.8xLLN (N=15,15,12,11)	0	0	0	0
Phosphate: >1.2xULN (N=15,15,12,11)	0	1	1	0
Bicarbonate (venous): <0.9xLLN (N=15,15,12,11)	9	11	7	3
Bicarbonate (venous): >1.1xULN (N=15,15,12,11)	0	0	0	0
Glucose: <0.6xLLN (N=15,15,12,11)	1	1	0	0
Glucose: >1.5xULN (N=15,15,12,11)	0	0	0	0

Insulin-like GrowthFactor:<0.9xLLN(N=12,13,11,10	0	0	1	0
Insulin-like GrowthFactor:>1.1xULN(N=12,13,11,10	5	8	4	6
IGF Binding Protein: <0.9xLLN (N=12,13,11,10)	0	0	0	0
IGF Binding Protein: >1.1xULN (N=12,13,11,10)	4	2	5	0
Lipid profile cholesterol/triglycerides(N=1,4,0,1)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Visit 1 to Visit 9 (Follow-up visit)

Adverse event reporting additional description:

The same event may appear as both an AE and a Serious Adverse Event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as non serious in another subject, or one subject may have experienced both a serious and non serious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Pregabalin: 1-23 Months

Reporting group description:

Age group included 1-23 months. Pregabalin was administered orally as liquid formulation at dose of 2.5, 5, 7.5, 10, or 15 mg/kg/day for 12 Months.

Reporting group title	Pregabalin: 2-6 Years

Reporting group description:

Age group included 2-6 years. Pregabalin was administered orally as liquid formulation at dose of 2.5, 5, 7.5, 10, or 15 mg/kg/day for 12 Months.

Reporting group title	Pregabalin: 7-11 Years

Reporting group description:

Age group included 7-11 years. Pregabalin was administered orally as capsule formulation and liquid formulation was used if subjects were unable to swallow capsules. Doses of 2.5, 5, 7.5, 10, or 15 mg/kg/day were given for 12 Months.

Reporting group title	Pregabalin: 12-16 Years

Reporting group description:

Age group included 12-16 years. Pregabalin was administered orally as capsule formulation and liquid formulation was used if subjects were unable to swallow capsules. Doses of 2.5, 5, 7.5, 10, or 15 mg/kg/day were given for 12 Months.

Reporting group title	Overall

Reporting group description:

This arm summarizes the AE data from all the treatment groups.

Serious adverse events	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 16 (50.00%)	3 / 15 (20.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			

subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 12 (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
Unresponsive to stimuli			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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			
Gastritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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
Ileus			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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
Salivary hypersecretion			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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
Respiratory, thoracic and mediastinal			

disorders			
Apnoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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
Bronchial hyperreactivity			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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
Respiratory distress			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (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
Respiratory failure			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Croup infectious			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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
Otitis media acute			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 12 (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
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (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 respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (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

Serious adverse events	Pregabalin: 12-16 Years	Overall	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	12 / 54 (22.22%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unresponsive to stimuli			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salivary hypersecretion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Croup infectious			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Otitis media acute			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pregabalin: 1-23 Months	Pregabalin: 2-6 Years	Pregabalin: 7-11 Years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 16 (87.50%)	13 / 15 (86.67%)	11 / 12 (91.67%)
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Crying			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Fatigue			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Pyrexia			
subjects affected / exposed	9 / 16 (56.25%)	3 / 15 (20.00%)	0 / 12 (0.00%)
occurrences (all)	17	5	0
Thirst			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	4 / 16 (25.00%)	2 / 15 (13.33%)	0 / 12 (0.00%)
occurrences (all)	5	2	0
Epistaxis			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	1 / 12 (8.33%)
occurrences (all)	0	3	1
Hypoxia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	2 / 16 (12.50%)	3 / 15 (20.00%)	1 / 12 (8.33%)
occurrences (all)	2	5	1
Productive cough			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Respiratory distress			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			

subjects affected / exposed	1 / 16 (6.25%)	2 / 15 (13.33%)	0 / 12 (0.00%)
occurrences (all)	1	2	0
Rhonchi			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Snoring			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anger			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dissociation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dysphemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dyssomnia			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hallucination, visual			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	2
Personality change			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Restlessness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Anticonvulsant drug level increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Weight increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Anal injury			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Arthropod bite			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Arthropod sting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Excoriation			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Foot fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Convulsion			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	3 / 12 (25.00%)
occurrences (all)	5	1	3
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Headache			

subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Lethargy			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Partial seizures			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Status epilepticus			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Cyclic neutropenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Leukocytosis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Thrombocytosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Astigmatism			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Excessive eye blinking			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypermetropia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Abdominal tenderness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	5 / 16 (31.25%)	1 / 15 (6.67%)	1 / 12 (8.33%)
occurrences (all)	7	1	1
Diarrhoea			
subjects affected / exposed	3 / 16 (18.75%)	3 / 15 (20.00%)	0 / 12 (0.00%)
occurrences (all)	4	4	0
Faeces pale			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Retching			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tooth impacted			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	3	1	0
Abdominal pain			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dermatitis diaper			
subjects affected / exposed	3 / 16 (18.75%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	3	1	0
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	2 / 16 (12.50%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Urine odour abnormal			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Muscle twitching			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal pain			

subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	0 / 16 (0.00%)	4 / 15 (26.67%)	1 / 12 (8.33%)
occurrences (all)	0	9	1
Eye infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Hordeolum			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 16 (18.75%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	5	0	0
Otitis media			
subjects affected / exposed	4 / 16 (25.00%)	4 / 15 (26.67%)	0 / 12 (0.00%)
occurrences (all)	13	6	0
Otitis media acute			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	2	1	0

Pharyngitis streptococcal			
subjects affected / exposed	0 / 16 (0.00%)	2 / 15 (13.33%)	1 / 12 (8.33%)
occurrences (all)	0	2	1
Pharyngotonsillitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Sinusitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Tinea infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 16 (18.75%)	5 / 15 (33.33%)	2 / 12 (16.67%)
occurrences (all)	8	8	2
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 15 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 16 (12.50%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	2	1	0
Hyperkalaemia			

subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Metabolic acidosis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 15 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Polydipsia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 15 (6.67%)	0 / 12 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	Pregabalin: 12-16 Years	Overall	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)	47 / 54 (87.04%)	
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Crying			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Irritability			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	4	
Pyrexia			
subjects affected / exposed	3 / 11 (27.27%)	15 / 54 (27.78%)	
occurrences (all)	3	25	
Thirst			

subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	0 / 11 (0.00%)	6 / 54 (11.11%)	
occurrences (all)	0	7	
Epistaxis			
subjects affected / exposed	1 / 11 (9.09%)	4 / 54 (7.41%)	
occurrences (all)	1	5	
Hypoxia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)	6 / 54 (11.11%)	
occurrences (all)	0	8	
Productive cough			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Respiratory distress			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Rhonchi			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Snoring			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Upper-airway cough syndrome			

subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Anger			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Depression			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Dissociation			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Dysphemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Dyssomnia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Hallucination, visual			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	3	
Personality change			

subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Anticonvulsant drug level increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	2	
Weight increased			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Anal injury			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Arthropod sting			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Excoriation			
subjects affected / exposed	2 / 11 (18.18%)	2 / 54 (3.70%)	
occurrences (all)	2	2	
Fall			

subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Foot fracture			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Laceration			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Convulsion			
subjects affected / exposed	1 / 11 (9.09%)	7 / 54 (12.96%)	
occurrences (all)	1	10	
Dizziness			
subjects affected / exposed	1 / 11 (9.09%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Headache			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	2	
Lethargy			
subjects affected / exposed	1 / 11 (9.09%)	3 / 54 (5.56%)	
occurrences (all)	1	3	
Partial seizures			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Somnolence			

subjects affected / exposed	1 / 11 (9.09%)	4 / 54 (7.41%)	
occurrences (all)	1	4	
Status epilepticus			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Cyclic neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Thrombocytosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 11 (9.09%)	2 / 54 (3.70%)	
occurrences (all)	1	2	
Eye disorders			
Astigmatism			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Excessive eye blinking			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Hypermetropia			

subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Abdominal tenderness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	7 / 54 (12.96%)	
occurrences (all)	0	9	
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	6 / 54 (11.11%)	
occurrences (all)	0	8	
Faeces pale			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Retching			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Salivary hypersecretion			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Tooth impacted			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	1 / 11 (9.09%)	4 / 54 (7.41%)	
occurrences (all)	1	5	
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	

Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Dermatitis diaper			
subjects affected / exposed	0 / 11 (0.00%)	4 / 54 (7.41%)	
occurrences (all)	0	4	
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Urine odour abnormal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Muscle twitching			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	2	
Infections and infestations			
Bacterial sepsis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Cystitis			

subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)		
occurrences (all)	1	1		
Device related infection				
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)		
occurrences (all)	0	1		
Ear infection				
subjects affected / exposed	0 / 11 (0.00%)	5 / 54 (9.26%)		
occurrences (all)	0	10		
Eye infection				
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)		
occurrences (all)	0	1		
Gastroenteritis				
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)		
occurrences (all)	0	2		
Hordeolum				
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)		
occurrences (all)	0	1		
Nasopharyngitis				
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)		
occurrences (all)	0	5		
Otitis media				
subjects affected / exposed	0 / 11 (0.00%)	8 / 54 (14.81%)		
occurrences (all)	0	19		
Otitis media acute				
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)		
occurrences (all)	0	3		
Pharyngitis streptococcal				
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)		
occurrences (all)	0	3		
Pharyngotonsillitis				
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)		
occurrences (all)	0	1		
Pneumonia				
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)		
occurrences (all)	0	1		
Rhinitis				

subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Staphylococcal infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Tinea infection			
subjects affected / exposed	1 / 11 (9.09%)	1 / 54 (1.85%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	10 / 54 (18.52%)	
occurrences (all)	0	18	
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)	3 / 54 (5.56%)	
occurrences (all)	0	3	
Hyperkalaemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Increased appetite			
subjects affected / exposed	0 / 11 (0.00%)	2 / 54 (3.70%)	
occurrences (all)	0	2	
Metabolic acidosis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	1	
Polydipsia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 54 (1.85%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 March 2011	1-Guidance provided to allow for reduction of blood volume required for subjects with low body weights in the 1-23 month infant cohort. 2-Language was added regarding handling of potential Hy's Law cases. Potential Hy's Law cases were reported as serious adverse events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported