Clinical trial results:
A Randomized, Double-Blind, Placebo Controlled, Fixed Dose-Ranging Study to Assess the Safety, Tolerability, and Efficacy of Topiramate Oral Liquid and Sprinkle Formulations as an Adjunct to Concurrent Anticonvulsant Therapy for Infants (1-24 Months of Age, Inclusive) With Refractory Partial-Onset Seizures, With Open-Label Extension

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2005-001338-33
Trial protocol	GB FI HU CZ ES NO BE IT
Global end of trial date	01 November 2007

Results information

Result version number	v2 (current)
This version publication date	01 July 2016
First version publication date	15 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	TOPMAT-PEP-3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00113815
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Johnson & Johnson Pharmaceutical Research & Development, L.L.C
Sponsor organisation address	Archimedsweg 29-2333CM, Leiden, Netherlands, B235-0
Public contact	Clinical Registry Group, Johnson & Johnson Pharmaceutical Research & Development, L.L.C, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Johnson & Johnson Pharmaceutical Research & Development, L.L.C, ClinicalTrialsEU@its.jnj.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	01 November 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 November 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to compare the effectiveness of topiramate 5, 15, or 25 milligram per kilogram per day (mg/kg/day) with that of placebo as an adjunct to concurrent anticonvulsant therapy in reducing daily partial onset seizure (POS) rates in infants (1 to 24 months of age, inclusive) with refractory POS after 20 days of double-blind treatment.

Protection of trial subjects:

The safety assessments included laboratory measurements (for example hematology, serum chemistry, and urinalysis), anthropometric measurements (body weight, body length, and head circumference), physical and neurological examinations, vineland scales of adaptive behavior, renal ultrasounds, vital sign measurements and electrocardiograms (ECGs). Adverse events were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 May 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 8
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	India: 76
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Norway: 2

Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Russian Federation: 31
Country: Number of subjects enrolled	South Africa: 2
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	Thailand: 1
Country: Number of subjects enrolled	Ukraine: 14
Country: Number of subjects enrolled	United States: 45
Worldwide total number of subjects	239
EEA total number of subjects	39

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)	236
Children (2-11 years)	3
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Double blind treatment: A total of 120 participants were planned, however 149 participants were enrolled and randomized in the study at 52 participating centers in 19 countries.
Open Label Phase: A total of 234 participants were enrolled.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants were received placebo oral solution/capsule orally twice daily for 20 Days.

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

Dosage and administration details:

Participants were received placebo oral solution twice daily for 20 Days.

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

Dosage and administration details:

Participants were received placebo capsule orally twice daily for 20 Days.

Arm title	Topiramate 5 milligram (mg)/killogram (kg)

Arm description:

Participants were received Topiramate 5 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.

Arm type	Experimental
Investigational medicinal product name	Topiramate Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate 5 milligram (mg) per killigram (kg) of body weight oral solution twice daily for 20 Days.

Investigational medicinal product name	Topiramate Sprinkle Capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate 5 milligram (mg) per killigram (kg) of body weight sprinkle capsule orally twice daily for 20 Days.

Arm title	Topiramate 15 milligram (mg)/killogram (kg)

Arm description:

Participants were received Topiramate 15 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.

Arm type	Experimental
Investigational medicinal product name	Topiramate Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate 15 milligram (mg) per killigram (kg) of body weight oral solution twice daily for 20 Days.

Investigational medicinal product name	Topiramate Sprinkle Capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate 15 milligram (mg) per killigram (kg) of body weight sprinkle capsule orally twice daily for 20 Days.

Arm title	Topiramate 25 milligram (mg)/killogram (kg)

Arm description:

Participants were received Topiramate 25 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.

Arm type	Experimental
Investigational medicinal product name	Topiramate Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate 25 milligram (mg) per killigram (kg) of body weight oral solution twice daily for 20 Days.

Investigational medicinal product name	Topiramate Sprinkle Capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate 25 milligram (mg) per killigram (kg) of body weight sprinkle capsule orally twice daily for 20 Days.

Arm title	Open Label Phase: Topiramate

Arm description:

Participants were received Topiramate up to 60 milligram (mg) per killigram (kg) of body weight oral

solution/sprinkle capsule orally twice daily for 1 Year.

Arm type	Experimental
Investigational medicinal product name	Topiramate Oral Solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate up to 60 milligram (mg) per killigram (kg) of body weight oral solution twice daily for 1 Year.

Investigational medicinal product name	Topiramate Sprinkle Capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were received Topiramate up to 60 milligram (mg) per killigram (kg) of body weight sprinkle capsule orally twice daily for 1 Year.

Number of subjects in period 1	Placebo	Topiramate 5 milligram (mg)/killogram (kg)	Topiramate 15 milligram (mg)/killogram (kg)
Started	37	38	37
Completed	29	34	33
Not completed	8	4	4
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	-	1
Other	4	3	2
Adverse event, serious non-fatal	-	-	-
Adverse event, serious non-fatal	1	1	1
Lost to follow-up	-	-	-
Lack of efficacy	1	-	-

Number of subjects in period 1	Topiramate 25 milligram (mg)/killogram (kg)	Open Label Phase: Topiramate
Started	37	90
Completed	34	57
Not completed	3	33
Adverse event, serious fatal	-	2
Consent withdrawn by subject	-	12
Adverse event, non-fatal	1	-
Other	2	11
Adverse event, serious non-fatal	-	2
Adverse event, serious non-fatal	-	-

Lost to follow-up	-	3
Lack of efficacy	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants were received placebo oral solution/capsule orally twice daily for 20 Days.	
Reporting group title	Topiramate 5 milligram (mg)/killogram (kg)
Reporting group description:	
Participants were received Topiramate 5 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.	
Reporting group title	Topiramate 15 milligram (mg)/killogram (kg)
Reporting group description:	
Participants were received Topiramate 15 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.	
Reporting group title	Topiramate 25 milligram (mg)/killogram (kg)
Reporting group description:	
Participants were received Topiramate 25 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.	
Reporting group title	Open Label Phase: Topiramate
Reporting group description:	
Participants were received Topiramate up to 60 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 1 Year.	

Reporting group values	Placebo	Topiramate 5 milligram (mg)/killogram (kg)	Topiramate 15 milligram (mg)/killogram (kg)
Number of subjects	37	38	37
Title for AgeCategorical Units: subjects			
infants and toddlers(28 days-23 months)	37	37	36
Children (2-11 years)	0	1	1
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: months			
arithmetic mean	11.8	13.3	12.4
standard deviation	± 5.91	± 7.56	± 6.15
Title for Gender Units: subjects			
Female	23	16	18
Male	14	22	19

Reporting group values	Topiramate 25 milligram (mg)/killogram (kg)	Open Label Phase: Topiramate	Total
Number of subjects	37	90	239
Title for AgeCategorical Units: subjects			
infants and toddlers(28 days-23 months)	37	89	236

Children (2-11 years)	0	1	3
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous			
Units: months			
arithmetic mean	10.2	12.7	
standard deviation	± 5.16	± 6.27	-
Title for Gender			
Units: subjects			
Female	14	40	111
Male	23	50	128

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants were received placebo oral solution/capsule orally twice daily for 20 Days.	
Reporting group title	Topiramate 5 milligram (mg)/killogram (kg)
Reporting group description:	
Participants were received Topiramate 5 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.	
Reporting group title	Topiramate 15 milligram (mg)/killogram (kg)
Reporting group description:	
Participants were received Topiramate 15 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.	
Reporting group title	Topiramate 25 milligram (mg)/killogram (kg)
Reporting group description:	
Participants were received Topiramate 25 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.	
Reporting group title	Open Label Phase: Topiramate
Reporting group description:	
Participants were received Topiramate up to 60 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 1 Year.	

Primary: Percentage Reduction in Daily Partial Onset Seizure Rate From Baseline to End of the Double Blind Phase

End point title	Percentage Reduction in Daily Partial Onset Seizure Rate From Baseline to End of the Double Blind Phase[1][2]
End point description:	
Daily partial onset seizure (POS) rate was evaluated based on video electroencephalogram (vEEG) data. For participants who had zero baseline seizure and the postseizure number is more than zero, value -8999 was imputed as the percent reduction in accordance with the worst-rank analysis.	
End point type	Primary
End point timeframe:	
Baseline and End of Double Blind Phase (Day 20)	

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: Descriptive statistics were done, no inferential statistical analyses were performed

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Placebo	Topiramate 5 milligram (mg)/killogram	Topiramate 15 milligram (mg)/killogram	Topiramate 25 milligram (mg)/killogram
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	34	34	34
Units: percentage (%)				
median (full range (min-max))	13.06 (-8999 to 100)	23.83 (-8999 to 100)	5.53 (-8999 to 100)	20.4 (-8999 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Treatment Responder Participants

End point title	Number of Treatment Responder Participants[3]

End point description:

A treatment responder was defined as a participant who had at least a 50 percent (%) reduction from baseline in seizure rate for a specific seizure type based on video electroencephalogram (vEEG) data.

End point type	Secondary

End point timeframe:

End of Double Blind Phase (Day 20)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Placebo	Topiramate 5 milligram (mg)/killogram	Topiramate 15 milligram (mg)/killogram	Topiramate 25 milligram (mg)/killogram
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	34	34	34
Units: Participants	10	9	13	15

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Reduction in Daily Seizure Rate for All Seizure Types From Baseline to End of the Double-Blind Phase

End point title	Percentage Reduction in Daily Seizure Rate for All Seizure Types From Baseline to End of the Double-Blind Phase[4]

End point description:

Daily Seizure Rate for All Seizure Types was evaluated based on video electroencephalogram (vEEG) data. For participants who had zero baseline seizure and the postseizure number is more than zero, value -8999 was imputed as the percent reduction in accordance with the worst-rank analysis.

End point type	Secondary

End point timeframe:

Baseline and End of Double Blind Phase (Day 20)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Placebo	Topiramate 5 milligram (mg)/killogram	Topiramate 15 milligram (mg)/killogram	Topiramate 25 milligram (mg)/killogram
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	34	34	34
Units: percentage (%)				
median (full range (min-max))	15.68 (-8999 to 100)	23.83 (-8999 to 100)	5.53 (-8999 to 100)	20.4 (-8999 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Reduction in Daily Seizure Rate for Partial Onset Seizure (POS) and All Seizure Types

End point title	Percent Reduction in Daily Seizure Rate for Partial Onset Seizure (POS) and All Seizure Types[5]

End point description:

Daily Seizure Rate for Partial Onset Seizure (POS) and All Seizure Types was evaluated based on participant take-home records. For participants who had zero baseline seizure and the postseizure number is more than zero, value -8999 was imputed as the percent reduction in accordance with the worst-rank analysis.

End point type	Secondary

End point timeframe:

Baseline and End of Double Blind Phase (Day 20)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be reported for the specific arms only

End point values	Placebo	Topiramate 5 milligram (mg)/killogram	Topiramate 15 milligram (mg)/killogram	Topiramate 25 milligram (mg)/killogram
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	38	37	37
Units: percentage (%)				
median (full range (min-max))	9.87 (-8999 to 97.7)	29.63 (-8999 to 100)	0.08 (-8999 to 100)	15.79 (-8999 to 100)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening up to follow-up (30 days after last treatment visit)

Assessment type	Non-systematic

Dictionary used

Dictionary name	WHOART
Dictionary version	SOC3

Reporting groups

Reporting group title	Open Label Phase: Placebo/Topiramate

Reporting group description:

Participants were received Placebo/Topiramate up to 60 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 1 Year.

Reporting group title	Open Label Phase: Topiramate

Reporting group description:

Participants were received Topiramate up to 60 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 1 Year.

Reporting group title	Open Label Phase: Topiramate/Topiramate

Reporting group description:

Participants were received Topiramate up to 60 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 1 Year.

Reporting group title	Double Blind Phase: Placebo

Reporting group description:

Participants were received placebo oral solution/capsule orally twice daily for 20 Days.

Reporting group title	Double Blind Phase: Topiramate 5 milligram (mg)/killogram (kg)

Reporting group description:

Participants were received Topiramate 5 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.

Reporting group title	Double Blind Phase: Topiramate 15 milligram (mg)/killogram(kg)

Reporting group description:

Participants were received Topiramate 15 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.

Reporting group title	Double Blind Phase: Topiramate 25 milligram (mg)/killogram(kg)

Reporting group description:

Participants were received Topiramate 25 milligram (mg) per killigram (kg) of body weight oral solution/sprinkle capsule orally twice daily for 20 Days.

Serious adverse events	Open Label Phase: Placebo/Topiramate	Open Label Phase: Topiramate	Open Label Phase: Topiramate/Topiramate
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 36 (47.22%)	34 / 90 (37.78%)	45 / 108 (41.67%)
number of deaths (all causes)	0	2	6
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Neoplasm Nos			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arteritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adverse Event Nos			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	1 / 36 (2.78%)	4 / 90 (4.44%)	5 / 108 (4.63%)
occurrences causally related to treatment / all	0 / 1	0 / 4	5 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Simplex			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Hypovolaemia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Infection			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	4 / 108 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infection Viral			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	5 / 108 (4.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 36 (5.56%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Unexpected Therapeutic Effect			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchitis			
subjects affected / exposed	0 / 36 (0.00%)	3 / 90 (3.33%)	7 / 108 (6.48%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	2 / 36 (5.56%)	1 / 90 (1.11%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Laryngitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	0 / 108 (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
Pharyngitis			
subjects affected / exposed	1 / 36 (2.78%)	4 / 90 (4.44%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	4 / 36 (11.11%)	9 / 90 (10.00%)	8 / 108 (7.41%)
occurrences causally related to treatment / all	0 / 4	0 / 15	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Pneumonitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 90 (1.11%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory Disorder			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Insufficiency			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Stridor			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Resp Tract Infection			
subjects affected / exposed	1 / 36 (2.78%)	6 / 90 (6.67%)	3 / 108 (2.78%)
occurrences causally related to treatment / all	0 / 2	0 / 8	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Anorexia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	1 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiomegaly			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory Failure			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsions			
subjects affected / exposed	1 / 36 (2.78%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsions Aggravated			
subjects affected / exposed	4 / 36 (11.11%)	9 / 90 (10.00%)	11 / 108 (10.19%)
occurrences causally related to treatment / all	1 / 7	1 / 16	9 / 23
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Convulsions Grand Mal			
subjects affected / exposed	1 / 36 (2.78%)	4 / 90 (4.44%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever Convulsions			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Gait Abnormal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulocytopenia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Leucopenia			

subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Lymphadenopathy			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Thrombocytopenia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 36 (2.78%)	3 / 90 (3.33%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	1 / 36 (2.78%)	1 / 90 (1.11%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	3 / 36 (8.33%)	3 / 90 (3.33%)	8 / 108 (7.41%)
occurrences causally related to treatment / all	0 / 3	0 / 3	1 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Gastroesophageal Reflux			

subjects affected / exposed	1 / 36 (2.78%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingivitis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Haematemesis			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	0 / 108 (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
Vomiting			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic Enzymes Increased			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (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
Hepatocellular Damage			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal Calculus			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection			
subjects affected / exposed	0 / 36 (0.00%)	2 / 90 (2.22%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone Development Abnormal			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 36 (2.78%)	0 / 90 (0.00%)	0 / 108 (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
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 36 (2.78%)	2 / 90 (2.22%)	4 / 108 (3.70%)
occurrences causally related to treatment / all	0 / 1	3 / 3	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 36 (2.78%)	3 / 90 (3.33%)	3 / 108 (2.78%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Growth Retarded			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hyperammonaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	2 / 108 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	1 / 108 (0.93%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight Decrease			
subjects affected / exposed	0 / 36 (0.00%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Double Blind Phase: Placebo	Double Blind Phase: Topiramate 5 milligram (mg)/killogram (kg)	Double Blind Phase: Topiramate 15 milligram (mg)/killogram(kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 37 (8.11%)	3 / 38 (7.89%)	4 / 37 (10.81%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm Nos			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Vascular disorders			
Arteritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
General disorders and administration site conditions			
Adverse Event Nos			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Fatigue			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Fever			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Herpes Simplex			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Hypovolaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection Viral			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 37 (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
Injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Otitis Media			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Sepsis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Unexpected Therapeutic Effect			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Bronchospasm			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Laryngitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 37 (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
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Pneumonia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Insufficiency			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Stridor			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Upper Resp Tract Infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Psychiatric disorders			
Anorexia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Somnolence			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Cardiomegaly			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Circulatory Failure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Convulsions			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Convulsions Aggravated			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsions Grand Mal			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	0 / 37 (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	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Encephalopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Fever Convulsions			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Gait Abnormal			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Meningitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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			
Anaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Granulocytopenia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Leucopenia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Lymphadenopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Thrombocytopenia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Gastrointestinal disorders			

Abdominal Pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Diarrhoea			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Enterocolitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Gastritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Gastroesophageal Reflux			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Gingivitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Haematemesis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Hepatobiliary disorders			
Hepatic Enzymes Increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Hepatocellular Damage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Renal Calculus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Urinary Tract Infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Musculoskeletal and connective tissue disorders			
Bone Development Abnormal			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Osteomyelitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Dehydration			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Growth Retarded			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Hyperammonaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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
Weight Decrease			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (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

Serious adverse events	Double Blind Phase: Topiramate 25 milligram (mg)/killogram(kg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 37 (10.81%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm Nos			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arteritis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Adverse Event Nos			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes Simplex			

subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypovolaemia				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection Viral				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis Media				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Unexpected Therapeutic Effect				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Aspiration				

subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 37 (5.41%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngitis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	1 / 37 (2.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Disorder				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Insufficiency				

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stridor			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper Resp Tract Infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anorexia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Somnolence			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiomegaly			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Circulatory Failure			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Ataxia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Convulsions			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Convulsions Aggravated			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Convulsions Grand Mal			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fever Convulsions			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gait Abnormal			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Granulocytopenia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leucopenia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenopathy			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			

subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroesophageal Reflux				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gingivitis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic Enzymes Increased				
subjects affected / exposed	0 / 37 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatocellular Damage				

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal Calculus			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone Development Abnormal			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Acidosis			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cachexia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Growth Retarded			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperammonaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Weight Decrease			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Open Label Phase: Placebo/Topiramate	Open Label Phase: Topiramate	Open Label Phase: Topiramate/Topiramate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 36 (91.67%)	84 / 90 (93.33%)	105 / 108 (97.22%)
Nervous system disorders			
Convulsions Aggravated			
subjects affected / exposed	4 / 36 (11.11%)	11 / 90 (12.22%)	21 / 108 (19.44%)
occurrences (all)	7	17	52
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 36 (5.56%)	4 / 90 (4.44%)	5 / 108 (4.63%)
occurrences (all)	4	6	9
General disorders and administration site conditions			
Fever			
subjects affected / exposed	18 / 36 (50.00%)	48 / 90 (53.33%)	47 / 108 (43.52%)
occurrences (all)	51	121	113
Infection			
subjects affected / exposed	3 / 36 (8.33%)	0 / 90 (0.00%)	3 / 108 (2.78%)
occurrences (all)	3	0	3
Infection Viral			
subjects affected / exposed	10 / 36 (27.78%)	23 / 90 (25.56%)	20 / 108 (18.52%)
occurrences (all)	21	33	37
Injury			
subjects affected / exposed	4 / 36 (11.11%)	8 / 90 (8.89%)	4 / 108 (3.70%)
occurrences (all)	9	12	4
Otitis Media			
subjects affected / exposed	2 / 36 (5.56%)	19 / 90 (21.11%)	8 / 108 (7.41%)
occurrences (all)	3	42	25
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 36 (2.78%)	8 / 90 (8.89%)	7 / 108 (6.48%)
occurrences (all)	2	13	9
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 36 (8.33%)	8 / 90 (8.89%)	9 / 108 (8.33%)
occurrences (all)	7	14	15
Diarrhoea			

subjects affected / exposed	9 / 36 (25.00%)	22 / 90 (24.44%)	23 / 108 (21.30%)
occurrences (all)	11	29	46
Gastroenteritis			
subjects affected / exposed	5 / 36 (13.89%)	12 / 90 (13.33%)	13 / 108 (12.04%)
occurrences (all)	5	12	16
Gastroesophageal Reflux			
subjects affected / exposed	2 / 36 (5.56%)	2 / 90 (2.22%)	1 / 108 (0.93%)
occurrences (all)	2	2	1
Mouth Dry			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	0 / 108 (0.00%)
occurrences (all)	0	0	0
Saliva Increased			
subjects affected / exposed	2 / 36 (5.56%)	1 / 90 (1.11%)	0 / 108 (0.00%)
occurrences (all)	2	1	0
Tooth Disorder			
subjects affected / exposed	3 / 36 (8.33%)	10 / 90 (11.11%)	0 / 108 (0.00%)
occurrences (all)	9	14	0
Vomiting			
subjects affected / exposed	11 / 36 (30.56%)	15 / 90 (16.67%)	26 / 108 (24.07%)
occurrences (all)	38	18	95
Respiratory, thoracic and mediastinal disorders			
Bronchitis			
subjects affected / exposed	7 / 36 (19.44%)	9 / 90 (10.00%)	18 / 108 (16.67%)
occurrences (all)	11	13	45
Bronchospasm			
subjects affected / exposed	0 / 36 (0.00%)	8 / 90 (8.89%)	3 / 108 (2.78%)
occurrences (all)	0	13	8
Coughing			
subjects affected / exposed	6 / 36 (16.67%)	14 / 90 (15.56%)	19 / 108 (17.59%)
occurrences (all)	8	23	26
Pharyngitis			
subjects affected / exposed	7 / 36 (19.44%)	10 / 90 (11.11%)	5 / 108 (4.63%)
occurrences (all)	7	20	12
Pneumonia			

subjects affected / exposed	3 / 36 (8.33%)	6 / 90 (6.67%)	3 / 108 (2.78%)
occurrences (all)	3	7	3
Respiratory Disorder			
subjects affected / exposed	2 / 36 (5.56%)	3 / 90 (3.33%)	1 / 108 (0.93%)
occurrences (all)	2	5	1
Rhinitis			
subjects affected / exposed	6 / 36 (16.67%)	17 / 90 (18.89%)	13 / 108 (12.04%)
occurrences (all)	11	33	20
Sinusitis			
subjects affected / exposed	0 / 36 (0.00%)	5 / 90 (5.56%)	2 / 108 (1.85%)
occurrences (all)	0	12	5
Upper Resp Tract Infection			
subjects affected / exposed	13 / 36 (36.11%)	50 / 90 (55.56%)	41 / 108 (37.96%)
occurrences (all)	42	174	132
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	3 / 36 (8.33%)	8 / 90 (8.89%)	8 / 108 (7.41%)
occurrences (all)	3	12	9
Dermatitis Contact			
subjects affected / exposed	0 / 36 (0.00%)	3 / 90 (3.33%)	1 / 108 (0.93%)
occurrences (all)	0	7	1
Rash			
subjects affected / exposed	2 / 36 (5.56%)	5 / 90 (5.56%)	9 / 108 (8.33%)
occurrences (all)	3	8	16
Rash Maculo-Papular			
subjects affected / exposed	1 / 36 (2.78%)	0 / 90 (0.00%)	5 / 108 (4.63%)
occurrences (all)	1	0	9
Skin Dry			
subjects affected / exposed	1 / 36 (2.78%)	0 / 90 (0.00%)	3 / 108 (2.78%)
occurrences (all)	1	0	4
Psychiatric disorders			
Anorexia			
subjects affected / exposed	7 / 36 (19.44%)	32 / 90 (35.56%)	31 / 108 (28.70%)
occurrences (all)	10	74	57
Insomnia			

subjects affected / exposed	1 / 36 (2.78%)	10 / 90 (11.11%)	4 / 108 (3.70%)
occurrences (all)	2	19	6
Nervousness			
subjects affected / exposed	4 / 36 (11.11%)	16 / 90 (17.78%)	8 / 108 (7.41%)
occurrences (all)	11	29	13
Somnolence			
subjects affected / exposed	7 / 36 (19.44%)	22 / 90 (24.44%)	18 / 108 (16.67%)
occurrences (all)	13	52	38
Renal and urinary disorders			
Renal Calculus			
subjects affected / exposed	2 / 36 (5.56%)	4 / 90 (4.44%)	5 / 108 (4.63%)
occurrences (all)	3	8	7
Urinary Tract Infection			
subjects affected / exposed	0 / 36 (0.00%)	7 / 90 (7.78%)	4 / 108 (3.70%)
occurrences (all)	0	9	5
Infections and infestations			
Vaginitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 90 (0.00%)	0 / 108 (0.00%)
occurrences (all)	3	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	13 / 36 (36.11%)	22 / 90 (24.44%)	31 / 108 (28.70%)
occurrences (all)	20	37	64
Growth Retarded			
subjects affected / exposed	0 / 36 (0.00%)	0 / 90 (0.00%)	9 / 108 (8.33%)
occurrences (all)	0	0	14
Hyperammonaemia			
subjects affected / exposed	2 / 36 (5.56%)	3 / 90 (3.33%)	8 / 108 (7.41%)
occurrences (all)	4	4	14
Hyperchloraemia			
subjects affected / exposed	1 / 36 (2.78%)	1 / 90 (1.11%)	4 / 108 (3.70%)
occurrences (all)	1	1	5
Weight Decrease			
subjects affected / exposed	3 / 36 (8.33%)	9 / 90 (10.00%)	20 / 108 (18.52%)
occurrences (all)	10	19	40

Non-serious adverse events	Double Blind Phase:	Double Blind Phase:	Double Blind Phase:

	Placebo	Topiramate 5 milligram (mg)/killogram (kg)	Topiramate 15 milligram (mg)/killogram(kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 37 (51.35%)	29 / 38 (76.32%)	28 / 37 (75.68%)
Nervous system disorders			
Convulsions Aggravated			
subjects affected / exposed	1 / 37 (2.70%)	2 / 38 (5.26%)	0 / 37 (0.00%)
occurrences (all)	1	4	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fever			
subjects affected / exposed	4 / 37 (10.81%)	11 / 38 (28.95%)	9 / 37 (24.32%)
occurrences (all)	11	18	11
Infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Infection Viral			
subjects affected / exposed	0 / 37 (0.00%)	4 / 38 (10.53%)	0 / 37 (0.00%)
occurrences (all)	0	4	0
Injury			
subjects affected / exposed	1 / 37 (2.70%)	1 / 38 (2.63%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
Otitis Media			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	1 / 37 (2.70%)
occurrences (all)	0	4	1
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 37 (2.70%)	1 / 38 (2.63%)	0 / 37 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			

subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	4 / 37 (10.81%)
occurrences (all)	0	1	7
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Gastroesophageal Reflux			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Mouth Dry			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Saliva Increased			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Tooth Disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 37 (5.41%)	7 / 38 (18.42%)	3 / 37 (8.11%)
occurrences (all)	4	15	3
Respiratory, thoracic and mediastinal disorders			
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	3 / 38 (7.89%)	1 / 37 (2.70%)
occurrences (all)	0	5	1
Bronchospasm			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Coughing			
subjects affected / exposed	2 / 37 (5.41%)	2 / 38 (5.26%)	1 / 37 (2.70%)
occurrences (all)	2	4	1
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 37 (0.00%)
occurrences (all)	0	1	0
Pneumonia			

subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Respiratory Disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	1 / 37 (2.70%)
occurrences (all)	0	3	1
Sinusitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Upper Resp Tract Infection			
subjects affected / exposed	5 / 37 (13.51%)	10 / 38 (26.32%)	9 / 37 (24.32%)
occurrences (all)	8	14	13
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	2 / 37 (5.41%)
occurrences (all)	0	1	4
Dermatitis Contact			
subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	4	0	0
Rash			
subjects affected / exposed	0 / 37 (0.00%)	1 / 38 (2.63%)	1 / 37 (2.70%)
occurrences (all)	0	2	1
Rash Maculo-Papular			
subjects affected / exposed	2 / 37 (5.41%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	4	0	0
Skin Dry			
subjects affected / exposed	0 / 37 (0.00%)	2 / 38 (5.26%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Anorexia			
subjects affected / exposed	2 / 37 (5.41%)	4 / 38 (10.53%)	4 / 37 (10.81%)
occurrences (all)	3	6	11
Insomnia			

subjects affected / exposed	1 / 37 (2.70%)	1 / 38 (2.63%)	0 / 37 (0.00%)
occurrences (all)	1	2	0
Nervousness			
subjects affected / exposed	0 / 37 (0.00%)	3 / 38 (7.89%)	3 / 37 (8.11%)
occurrences (all)	0	3	8
Somnolence			
subjects affected / exposed	3 / 37 (8.11%)	3 / 38 (7.89%)	8 / 37 (21.62%)
occurrences (all)	5	5	13
Renal and urinary disorders			
Renal Calculus			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Vaginitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	5
Growth Retarded			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Hyperammonaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 38 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	0
Hyperchloraemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 38 (0.00%)	2 / 37 (5.41%)
occurrences (all)	2	0	2
Weight Decrease			
subjects affected / exposed	1 / 37 (2.70%)	1 / 38 (2.63%)	3 / 37 (8.11%)
occurrences (all)	2	2	6

Non-serious adverse events	Double Blind Phase:		

	Topiramate 25 milligram (mg)/killogram(kg)		
Total subjects affected by non-serious adverse events subjects affected / exposed	31 / 37 (83.78%)		
Nervous system disorders Convulsions Aggravated subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 37 (0.00%) 0		
General disorders and administration site conditions Fever subjects affected / exposed occurrences (all) Infection subjects affected / exposed occurrences (all) Infection Viral subjects affected / exposed occurrences (all) Injury subjects affected / exposed occurrences (all) Otitis Media subjects affected / exposed occurrences (all)	9 / 37 (24.32%) 11 0 / 37 (0.00%) 0 3 / 37 (8.11%) 4 1 / 37 (2.70%) 2 2 / 37 (5.41%) 5		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 37 (2.70%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea	1 / 37 (2.70%) 1		

subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	4		
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Gastroesophageal Reflux			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Mouth Dry			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	3		
Saliva Increased			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	3		
Tooth Disorder			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	6 / 37 (16.22%)		
occurrences (all)	10		
Respiratory, thoracic and mediastinal disorders			
Bronchitis			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	9		
Bronchospasm			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	2		
Coughing			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	6		
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Pneumonia			

subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Respiratory Disorder			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Upper Resp Tract Infection			
subjects affected / exposed	8 / 37 (21.62%)		
occurrences (all)	14		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Dermatitis Contact			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Rash Maculo-Papular			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Skin Dry			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anorexia			
subjects affected / exposed	8 / 37 (21.62%)		
occurrences (all)	11		
Insomnia			

subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Nervousness			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Somnolence			
subjects affected / exposed	6 / 37 (16.22%)		
occurrences (all)	11		
Renal and urinary disorders			
Renal Calculus			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Vaginitis			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	3 / 37 (8.11%)		
occurrences (all)	4		
Growth Retarded			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	2		
Hyperammonaemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Hyperchloraemia			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Weight Decrease			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2005	The overall reason for the amendment was to clarify exclusion criteria relating to seizure history and study procedures, including adjustment of blood volumes drawn, study drug storage conditions, entry into the open-label extension, and special instructions for prematurely born participants. One of the secondary efficacy variables of the statistical analysis was modified (included all seizure types), instructions for manual assignment to the open-label extension phase prior to starting the interactive voice response system (IVRS) were provided, and other minor errors were corrected.
15 April 2005	The overall reason for the amendment was to include additional safety measures or precautions, such as measurement of blood pressure, age limitation for enrollment, and documentation of inadequacy of current epilepsy treatment.
03 May 2006	The overall reason for the amendment was to incorporate investigator and regulatory authority feedback.
14 February 2007	The overall reason for the amendment was to write in response to a request from the United States Food and Drug Administration to reverse parts of Amendment INT-3. The time required after rescue treatment before the video electroencephalogram (vEEG) could begin was decreased from 48 to 12 hours in Amendment INT-3 and changed back to at least 48 hours after any rescue treatment with this amendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported