



## Clinical trial results:

### A Randomized, Double-Blind, Parallel-Group, Multicenter Study to Evaluate the Retention Rate, Efficacy, Safety, and Tolerability of Carisbamate, Topiramate and Levetiracetam as Adjunctive Therapy in Subjects With Partial Onset Seizures

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

## Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2007-002929-78          |
| Trial protocol           | GB CZ BE FI FR IT ES PT |
| Global end of trial date | 09 May 2010             |

## Results information

|                                |                                                                                                    |
|--------------------------------|----------------------------------------------------------------------------------------------------|
| Result version number          | v2 (current)                                                                                       |
| This version publication date  | 02 June 2016                                                                                       |
| First version publication date | 01 August 2015                                                                                     |
| Version creation reason        | <ul style="list-style-type: none"><li>Correction of full data set</li><li>Review of data</li></ul> |

## Trial information

### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CARISEPY3007 |
|-----------------------|--------------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00563459 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |                                                                                                                          |
|------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Ortho-McNeil Janssen Scientific Affairs, LLC                                                                             |
| Sponsor organisation address | 1125 Trenton-Harbourton Road, Titusville, NJ 08560, United States,                                                       |
| Public contact               | Ortho-McNeil Janssen Scientific Affairs, LLC, Ortho-McNeil Janssen Scientific Affairs, LLC, ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Ortho-McNeil Janssen Scientific Affairs, LLC, Ortho-McNeil Janssen Scientific Affairs, LLC, 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                       | 09 May 2010 |
| Is this the analysis of the primary completion data? | No          |
| Global end of trial reached?                         | Yes         |
| Global end of trial date                             | 09 May 2010 |
| Was the trial ended prematurely?                     | No          |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the long-term retention rate of carisbamate (CRS) versus topiramate (TPM) and levetiracetam (LEV) when given adjunctively to subjects with partial onset seizures based on discontinuations due to all causes over a 6-month period.

Protection of trial subjects:

An independent Data Safety Monitoring Board (DSMB) met during the course of the study to ensure the safety of the subjects and monitor any clinically relevant trends. Safety and tolerability evaluations included monitoring of the frequency, severity, and timing of adverse events (AEs), clinical laboratory test values, liver function tests, serum lipid profiles, urine drug screen, 12-lead electrocardiogram (ECG) recordings, vital signs measurements, physical and neurologic examinations, study drug levels and concomitant adjunctive antiepileptic drug (AED) levels, and pregnancy tests for females of childbearing potential.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 05 November 2007 |
| 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 | Czech Republic: 4      |
| Country: Number of subjects enrolled | Mexico: 11             |
| Country: Number of subjects enrolled | Poland: 20             |
| Country: Number of subjects enrolled | Korea, Republic of: 9  |
| Country: Number of subjects enrolled | Russian Federation: 10 |
| Country: Number of subjects enrolled | South Africa: 4        |
| Country: Number of subjects enrolled | United States: 31      |
| Worldwide total number of subjects   | 89                     |
| EEA total number of subjects         | 24                     |

Notes:

**Subjects enrolled per age group**

|                                           |    |
|-------------------------------------------|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 2  |
| Adults (18-64 years)                      | 84 |
| From 65 to 84 years                       | 3  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 600 subjects were to be enrolled (200 subjects in each group) initially. At study termination, 89 subjects had been randomly assigned to treatment (29, 29, and 31 subjects in the CRS versus TPM and LEV groups, respectively).

### Pre-assignment

Screening details:

Across all treatment groups, of the 89 subjects who were randomly assigned to treatment and received at least 1 dose of study drug, 60 subjects completed the 6-month core double-blind phase (17 CRS, 19 TPM, and 24 LEV) and 5 subjects (2 CRS, 2 TPM, and 1 LEV) completed the 12-month double-blind phase; Only 9 subjects had begun the open-label phase.

### 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, Carer   |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Carisbamate |

Arm description:

The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 milligram per day (mg/day).

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Carisbamate  |
| Investigational medicinal product code | RWJ-333369   |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 mg/day.

|                  |            |
|------------------|------------|
| <b>Arm title</b> | Topiramate |
|------------------|------------|

Arm description:

The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Topiramate        |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Levetiracetam |
|------------------|---------------|

Arm description:

The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.

|          |                   |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

|                                        |               |
|----------------------------------------|---------------|
| Investigational medicinal product name | levetiracetam |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule       |
| Routes of administration               | Oral use      |

Dosage and administration details:

The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.

| <b>Number of subjects in period 1</b>             | Carisbamate | Topiramate | Levetiracetam |
|---------------------------------------------------|-------------|------------|---------------|
| Started                                           | 29          | 29         | 31            |
| Completed                                         | 2           | 2          | 1             |
| Not completed                                     | 27          | 27         | 30            |
| Consent withdrawn by subject                      | 4           | 4          | -             |
| Adverse event, non-fatal                          | -           | 4          | 2             |
| Non compliance                                    | -           | -          | 2             |
| Insufficient seizure control                      | 5           | 1          | 2             |
| Lost to follow-up                                 | -           | 2          | -             |
| Discontinuation due to early termination of study | 18          | 16         | 24            |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                |               |
|------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title                                                                                                                          | Carisbamate   |
| Reporting group description:<br>The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 milligram per day (mg/day). |               |
| Reporting group title                                                                                                                          | Topiramate    |
| Reporting group description:<br>The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.                        |               |
| Reporting group title                                                                                                                          | Levetiracetam |
| Reporting group description:<br>The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.                 |               |

| Reporting group values                      | Carisbamate | Topiramate | Levetiracetam |
|---------------------------------------------|-------------|------------|---------------|
| Number of subjects                          | 29          | 29         | 31            |
| Title for AgeCategorical<br>Units: subjects |             |            |               |
| Children (2-11 years)                       | 0           | 0          | 0             |
| Adolescents (12-17 years)                   | 0           | 1          | 1             |
| Adults (18-64 years)                        | 28          | 27         | 29            |
| From 65 to 84 years                         | 1           | 1          | 1             |
| 85 years and over                           | 0           | 0          | 0             |
| Title for AgeContinuous<br>Units: years     |             |            |               |
| arithmetic mean                             | 37.9        | 38.3       | 39.8          |
| standard deviation                          | ± 11.82     | ± 15.12    | ± 13.11       |
| Title for Gender<br>Units: subjects         |             |            |               |
| Female                                      | 18          | 10         | 15            |
| Male                                        | 11          | 19         | 16            |

| Reporting group values                      | Total |  |  |
|---------------------------------------------|-------|--|--|
| Number of subjects                          | 89    |  |  |
| Title for AgeCategorical<br>Units: subjects |       |  |  |
| Children (2-11 years)                       | 0     |  |  |
| Adolescents (12-17 years)                   | 2     |  |  |
| Adults (18-64 years)                        | 84    |  |  |
| From 65 to 84 years                         | 3     |  |  |
| 85 years and over                           | 0     |  |  |
| Title for AgeContinuous<br>Units: years     |       |  |  |
| arithmetic mean                             |       |  |  |
| standard deviation                          | -     |  |  |
| Title for Gender<br>Units: subjects         |       |  |  |
| Female                                      | 43    |  |  |
| Male                                        | 46    |  |  |



## End points

### End points reporting groups

|                                                                                                                                                |               |
|------------------------------------------------------------------------------------------------------------------------------------------------|---------------|
| Reporting group title                                                                                                                          | Carisbamate   |
| Reporting group description:<br>The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 milligram per day (mg/day). |               |
| Reporting group title                                                                                                                          | Topiramate    |
| Reporting group description:<br>The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day.                        |               |
| Reporting group title                                                                                                                          | Levetiracetam |
| Reporting group description:<br>The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day.                 |               |

### Primary: Time From the First Intake of Study Medication to Discontinuation (all causes) of Study Medication During the 6 Month Core Double-Blind Phase

|                                                                                                                                                                                                                                                                                      |                                                                                                                                                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                      | Time From the First Intake of Study Medication to Discontinuation (all causes) of Study Medication During the 6 Month Core Double-Blind Phase <sup>[1]</sup> |
| End point description:<br>Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated.                                                                                                                                   |                                                                                                                                                              |
| End point type                                                                                                                                                                                                                                                                       | Primary                                                                                                                                                      |
| End point timeframe:<br>Baseline up to month 6                                                                                                                                                                                                                                       |                                                                                                                                                              |
| Notes:<br>[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.<br>Justification: Descriptive statistics were done, no inferential statistical analyses were performed |                                                                                                                                                              |

| End point values              | Carisbamate      | Topiramate       | Levetiracetam    |  |
|-------------------------------|------------------|------------------|------------------|--|
| Subject group type            | Reporting group  | Reporting group  | Reporting group  |  |
| Number of subjects analysed   | 0 <sup>[2]</sup> | 0 <sup>[3]</sup> | 0 <sup>[4]</sup> |  |
| Units: Days                   |                  |                  |                  |  |
| median (full range (min-max)) | ( to )           | ( to )           | ( to )           |  |

Notes:

[2] - Due to early termination, no subject was analyzed for this endpoint.

[3] - Due to early termination, no subject was analyzed for this endpoint.

[4] - Due to early termination, no subject was analyzed for this endpoint.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Reasons For Discontinuation

|                                                                                                                     |                                                     |
|---------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| End point title                                                                                                     | Number of Subjects With Reasons For Discontinuation |
| End point description:<br>Randomized analysis set included all subjects who received at least 1 dose of study drug. |                                                     |
| End point type                                                                                                      | Secondary                                           |



End point timeframe:

Month 6 and 12

| End point values                             | Carisbamate     | Topiramate      | Levetiracetam   |  |
|----------------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type                           | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed                  | 29              | 29              | 31              |  |
| Units: Number                                |                 |                 |                 |  |
| Insufficient seizure control                 | 5               | 1               | 2               |  |
| Adverse event                                | 0               | 4               | 2               |  |
| Non-compliance                               | 0               | 0               | 2               |  |
| Lost to follow-up                            | 0               | 2               | 0               |  |
| Subject choice (subject withdrew consent)    | 4               | 4               | 0               |  |
| Pregnancy                                    | 0               | 0               | 0               |  |
| Death                                        | 0               | 0               | 0               |  |
| Other                                        | 18              | 16              | 24              |  |
| No. of subjects completed double blind phase | 2               | 2               | 1               |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with Seizures Rates Among the 3 Treatment Arms

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Number of Subjects with Seizures Rates Among the 3 Treatment Arms |
|-----------------|-------------------------------------------------------------------|

End point description:

Safety analysis set included all subjects who were randomized and received at least 1 dose of study medication.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Upto 12 months

| End point values                            | Carisbamate     | Topiramate      | Levetiracetam   |  |
|---------------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type                          | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed                 | 29              | 29              | 31              |  |
| Units: Subjects                             |                 |                 |                 |  |
| arithmetic mean (standard deviation)        |                 |                 |                 |  |
| Simple partial motor                        | 1.5 (± 3)       | 0.73 (± 2.85)   | 2.4 (± 6.78)    |  |
| Complex partial                             | 1.92 (± 2.79)   | 0.94 (± 1.81)   | 1.25 (± 2.95)   |  |
| Partial evolving to secondarily generalized | 0.44 (± 0.99)   | 0.49 (± 1.78)   | 0.24 (± 0.74)   |  |
| Other                                       | 0.01 (± 0.06)   | 0.16 (± 0.75)   | 0.69 (± 3.84)   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Cognitive Disorders With a Computerized Cognitive Test Battery Among the 3 Treatment Arms

|                 |                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------|
| End point title | Change From Baseline in Cognitive Disorders With a Computerized Cognitive Test Battery Among the 3 Treatment Arms |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

End point description:

Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline; Week 3, 7; Month 3, 6

| End point values                     | Carisbamate      | Topiramate       | Levetiracetam    |  |
|--------------------------------------|------------------|------------------|------------------|--|
| Subject group type                   | Reporting group  | Reporting group  | Reporting group  |  |
| Number of subjects analysed          | 0 <sup>[5]</sup> | 0 <sup>[6]</sup> | 0 <sup>[7]</sup> |  |
| Units: units on a scale              |                  |                  |                  |  |
| arithmetic mean (standard deviation) | ()               | ()               | ()               |  |

Notes:

[5] - Due to early termination, no subject was analyzed for this endpoint.

[6] - Due to early termination, no subject was analyzed for this endpoint.

[7] - Due to early termination, no subject was analyzed for this endpoint.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Neuropsychiatric side effect profiles of Carisbamate (CRS) and levetiracetam (LEV)

|                 |                                                                                    |
|-----------------|------------------------------------------------------------------------------------|
| End point title | Neuropsychiatric side effect profiles of Carisbamate (CRS) and levetiracetam (LEV) |
|-----------------|------------------------------------------------------------------------------------|

End point description:

Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 6 and 12

| End point values                     | Carisbamate      | Topiramate       | Levetiracetam     |  |
|--------------------------------------|------------------|------------------|-------------------|--|
| Subject group type                   | Reporting group  | Reporting group  | Reporting group   |  |
| Number of subjects analysed          | 0 <sup>[8]</sup> | 0 <sup>[9]</sup> | 0 <sup>[10]</sup> |  |
| Units: Units on a scale              |                  |                  |                   |  |
| arithmetic mean (standard deviation) | ()               | ()               | ()                |  |

Notes:

[8] - Due to early termination of study, no subject was analyzed in this endpoint.

[9] - Due to early termination of study, no subject was analyzed in this endpoint.

[10] - Due to early termination of study, no subject was analyzed in this endpoint.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Reported Cognitive and Psychiatric Disorders Among the 3 Treatment Arms Recorded as Treatment Emergent Adverse Events (TEAEs)

|                 |                                                                                                                                                  |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects Reported Cognitive and Psychiatric Disorders Among the 3 Treatment Arms Recorded as Treatment Emergent Adverse Events (TEAEs) |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

TEAEs in the double-blind phase are adverse events which started on or after the start of double-blind treatment and before the start of transition or open-label treatment, or within 14 days (30 days if serious) of the last dose of double-blind study drug if the subject did not take transition or open-label study drug. Safety analysis set included subjects who were randomly assigned to treatment and received at least 1 dose of study medication.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Month 6 and 12

| End point values            | Carisbamate     | Topiramate      | Levetiracetam   |  |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type          | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed | 29              | 29              | 31              |  |
| Units: subjects             |                 |                 |                 |  |
| Cognitive disorder          | 0               | 2               | 0               |  |
| Psychiatric disorder        | 3               | 4               | 5               |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 30 days after last dose of study drug

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Carisbamate |
|-----------------------|-------------|

Reporting group description:

The subjects who randomized to Carisbamate received dose ranging from 400 to 1,200 mg/day

|                       |               |
|-----------------------|---------------|
| Reporting group title | Levetiracetam |
|-----------------------|---------------|

Reporting group description:

The subjects who randomized to Levetiracetam received dose ranging from 1,000 to 3,000 mg/day

|                       |            |
|-----------------------|------------|
| Reporting group title | Topiramate |
|-----------------------|------------|

Reporting group description:

The subjects who randomized to Topiramate received dose ranging from 200 to 400 mg/day

| Serious adverse events                            | Carisbamate    | Levetiracetam  | Topiramate     |
|---------------------------------------------------|----------------|----------------|----------------|
| Total subjects affected by serious adverse events |                |                |                |
| subjects affected / exposed                       | 1 / 29 (3.45%) | 3 / 31 (9.68%) | 1 / 29 (3.45%) |
| number of deaths (all causes)                     | 0              | 1              | 0              |
| number of deaths resulting from adverse events    |                |                |                |
| Injury, poisoning and procedural complications    |                |                |                |
| Brain Contusion                                   |                |                |                |
| subjects affected / exposed                       | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Femoral Neck Fracture                             |                |                |                |
| subjects affected / exposed                       | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (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          |
| Muscle Strain                                     |                |                |                |
| subjects affected / exposed                       | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                                 |                |                |                |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Cardio-Respiratory Arrest                       |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (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          |
| Nervous system disorders                        |                |                |                |
| Cerebral Haemorrhage                            |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (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          |
| Epilepsy                                        |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events                                          | Carisbamate      | Levetiracetam    | Topiramate       |
|---------------------------------------------------------------------|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events               |                  |                  |                  |
| subjects affected / exposed                                         | 20 / 29 (68.97%) | 27 / 31 (87.10%) | 24 / 29 (82.76%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |                  |
| Skin Papilloma                                                      |                  |                  |                  |
| subjects affected / exposed                                         | 1 / 29 (3.45%)   | 0 / 31 (0.00%)   | 0 / 29 (0.00%)   |
| occurrences (all)                                                   | 1                | 0                | 0                |
| Vascular disorders                                                  |                  |                  |                  |
| Hypertension                                                        |                  |                  |                  |
| subjects affected / exposed                                         | 1 / 29 (3.45%)   | 1 / 31 (3.23%)   | 1 / 29 (3.45%)   |
| occurrences (all)                                                   | 1                | 1                | 1                |
| General disorders and administration site conditions                |                  |                  |                  |
| Asthenia                                                            |                  |                  |                  |

|                                                                                                               |                      |                      |                      |
|---------------------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                              | 2 / 29 (6.90%)<br>2  | 0 / 31 (0.00%)<br>0  | 2 / 29 (6.90%)<br>2  |
| Chills<br>subjects affected / exposed<br>occurrences (all)                                                    | 0 / 29 (0.00%)<br>0  | 1 / 31 (3.23%)<br>1  | 1 / 29 (3.45%)<br>1  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                                                   | 3 / 29 (10.34%)<br>4 | 3 / 31 (9.68%)<br>3  | 3 / 29 (10.34%)<br>3 |
| Gait Disturbance<br>subjects affected / exposed<br>occurrences (all)                                          | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1  |
| Influenza Like Illness<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 29 (0.00%)<br>0  | 1 / 31 (3.23%)<br>2  | 1 / 29 (3.45%)<br>1  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                                              | 1 / 29 (3.45%)<br>1  | 4 / 31 (12.90%)<br>4 | 1 / 29 (3.45%)<br>1  |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)                                         | 1 / 29 (3.45%)<br>3  | 0 / 31 (0.00%)<br>0  | 0 / 29 (0.00%)<br>0  |
| Pain<br>subjects affected / exposed<br>occurrences (all)                                                      | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                                                   | 0 / 29 (0.00%)<br>0  | 1 / 31 (3.23%)<br>1  | 1 / 29 (3.45%)<br>1  |
| Immune system disorders<br>Seasonal Allergy<br>subjects affected / exposed<br>occurrences (all)               | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1  |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all) | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0  | 1 / 29 (3.45%)<br>1  |
| Respiratory, thoracic and mediastinal disorders                                                               |                      |                      |                      |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Allergic Sinusitis          |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Dyspnoea                    |                |                |                |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 31 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Oropharyngeal Pain          |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 2 / 31 (6.45%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Pulmonary Congestion        |                |                |                |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 1              | 0              | 1              |
| Rhinitis Seasonal           |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Psychiatric disorders       |                |                |                |
| Abnormal Behaviour          |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 2 / 31 (6.45%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 2              | 1              |
| Aggression                  |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Agitation                   |                |                |                |
| subjects affected / exposed | 1 / 29 (3.45%) | 2 / 31 (6.45%) | 1 / 29 (3.45%) |
| occurrences (all)           | 1              | 2              | 2              |
| Anxiety                     |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 0              | 0              | 1              |
| Apathy                      |                |                |                |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Depression                  |                |                |                |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)           | 2              | 0              | 1              |
| Depressive Symptom          |                |                |                |

|                                        |                |                |                |
|----------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Hallucination                          |                |                |                |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 2              | 0              | 0              |
| Hostility                              |                |                |                |
| subjects affected / exposed            | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Insomnia                               |                |                |                |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)                      | 1              | 0              | 2              |
| Nightmare                              |                |                |                |
| subjects affected / exposed            | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Sleep Disorder                         |                |                |                |
| subjects affected / exposed            | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Investigations                         |                |                |                |
| Blood Creatine Phosphokinase Increased |                |                |                |
| subjects affected / exposed            | 0 / 29 (0.00%) | 2 / 31 (6.45%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 0              | 2              | 0              |
| Body Temperature Increased             |                |                |                |
| subjects affected / exposed            | 1 / 29 (3.45%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 2              | 1              | 0              |
| Electrocardiogram T Wave Inversion     |                |                |                |
| subjects affected / exposed            | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Liver Function Test Abnormal           |                |                |                |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Neutrophil Count Decreased             |                |                |                |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0              |
| Urine Analysis Abnormal                |                |                |                |



|                                                |                |                |                 |
|------------------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0               |
| Weight Decreased                               |                |                |                 |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 4 / 29 (13.79%) |
| occurrences (all)                              | 0              | 0              | 4               |
| Injury, poisoning and procedural complications |                |                |                 |
| Animal Bite                                    |                |                |                 |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0               |
| Back Injury                                    |                |                |                 |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0               |
| Contusion                                      |                |                |                 |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0               |
| Fall                                           |                |                |                 |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0               |
| Ligament Rupture                               |                |                |                 |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0               |
| Skin Laceration                                |                |                |                 |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0               |
| Stress Fracture                                |                |                |                 |
| subjects affected / exposed                    | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0               |
| Wound                                          |                |                |                 |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 1              | 0              | 0               |
| Cardiac disorders                              |                |                |                 |
| Angina Pectoris                                |                |                |                 |
| subjects affected / exposed                    | 1 / 29 (3.45%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                              | 1              | 1              | 0               |
| Bradycardia                                    |                |                |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 29 (0.00%)  | 1 / 31 (3.23%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Extrasystoles               |                 |                 |                 |
| subjects affected / exposed | 1 / 29 (3.45%)  | 0 / 31 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Palpitations                |                 |                 |                 |
| subjects affected / exposed | 0 / 29 (0.00%)  | 0 / 31 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Nervous system disorders    |                 |                 |                 |
| Aphasia                     |                 |                 |                 |
| subjects affected / exposed | 0 / 29 (0.00%)  | 0 / 31 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Cognitive Disorder          |                 |                 |                 |
| subjects affected / exposed | 0 / 29 (0.00%)  | 0 / 31 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)           | 0               | 0               | 2               |
| Balance Disorder            |                 |                 |                 |
| subjects affected / exposed | 0 / 29 (0.00%)  | 0 / 31 (0.00%)  | 1 / 29 (3.45%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Disturbance in Attention    |                 |                 |                 |
| subjects affected / exposed | 2 / 29 (6.90%)  | 0 / 31 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)           | 2               | 0               | 2               |
| Dizziness                   |                 |                 |                 |
| subjects affected / exposed | 6 / 29 (20.69%) | 4 / 31 (12.90%) | 5 / 29 (17.24%) |
| occurrences (all)           | 8               | 4               | 5               |
| Dizziness Postural          |                 |                 |                 |
| subjects affected / exposed | 1 / 29 (3.45%)  | 0 / 31 (0.00%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Dysarthria                  |                 |                 |                 |
| subjects affected / exposed | 0 / 29 (0.00%)  | 1 / 31 (3.23%)  | 0 / 29 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Headache                    |                 |                 |                 |
| subjects affected / exposed | 7 / 29 (24.14%) | 6 / 31 (19.35%) | 6 / 29 (20.69%) |
| occurrences (all)           | 26              | 7               | 16              |
| Hypersomnia                 |                 |                 |                 |
| subjects affected / exposed | 0 / 29 (0.00%)  | 0 / 31 (0.00%)  | 2 / 29 (6.90%)  |
| occurrences (all)           | 0               | 0               | 2               |

|                                      |                 |                  |                 |
|--------------------------------------|-----------------|------------------|-----------------|
| Hypokinesia                          |                 |                  |                 |
| subjects affected / exposed          | 1 / 29 (3.45%)  | 0 / 31 (0.00%)   | 0 / 29 (0.00%)  |
| occurrences (all)                    | 1               | 0                | 0               |
| Lethargy                             |                 |                  |                 |
| subjects affected / exposed          | 0 / 29 (0.00%)  | 0 / 31 (0.00%)   | 1 / 29 (3.45%)  |
| occurrences (all)                    | 0               | 0                | 1               |
| Memory Impairment                    |                 |                  |                 |
| subjects affected / exposed          | 2 / 29 (6.90%)  | 2 / 31 (6.45%)   | 2 / 29 (6.90%)  |
| occurrences (all)                    | 3               | 2                | 2               |
| Mental Impairment                    |                 |                  |                 |
| subjects affected / exposed          | 0 / 29 (0.00%)  | 2 / 31 (6.45%)   | 0 / 29 (0.00%)  |
| occurrences (all)                    | 0               | 2                | 0               |
| Myoclonus                            |                 |                  |                 |
| subjects affected / exposed          | 1 / 29 (3.45%)  | 0 / 31 (0.00%)   | 0 / 29 (0.00%)  |
| occurrences (all)                    | 2               | 0                | 0               |
| Paraesthesia                         |                 |                  |                 |
| subjects affected / exposed          | 0 / 29 (0.00%)  | 0 / 31 (0.00%)   | 8 / 29 (27.59%) |
| occurrences (all)                    | 0               | 0                | 13              |
| Psychomotor Hyperactivity            |                 |                  |                 |
| subjects affected / exposed          | 0 / 29 (0.00%)  | 1 / 31 (3.23%)   | 0 / 29 (0.00%)  |
| occurrences (all)                    | 0               | 1                | 0               |
| Somnolence                           |                 |                  |                 |
| subjects affected / exposed          | 6 / 29 (20.69%) | 11 / 31 (35.48%) | 3 / 29 (10.34%) |
| occurrences (all)                    | 6               | 11               | 3               |
| Speech Disorder                      |                 |                  |                 |
| subjects affected / exposed          | 0 / 29 (0.00%)  | 0 / 31 (0.00%)   | 1 / 29 (3.45%)  |
| occurrences (all)                    | 0               | 0                | 1               |
| Tremor                               |                 |                  |                 |
| subjects affected / exposed          | 3 / 29 (10.34%) | 0 / 31 (0.00%)   | 0 / 29 (0.00%)  |
| occurrences (all)                    | 3               | 0                | 0               |
| Blood and lymphatic system disorders |                 |                  |                 |
| Neutropenia                          |                 |                  |                 |
| subjects affected / exposed          | 0 / 29 (0.00%)  | 1 / 31 (3.23%)   | 0 / 29 (0.00%)  |
| occurrences (all)                    | 0               | 1                | 0               |
| Ear and labyrinth disorders          |                 |                  |                 |

|                                                                           |                     |                     |                     |
|---------------------------------------------------------------------------|---------------------|---------------------|---------------------|
| Vertigo<br>subjects affected / exposed<br>occurrences (all)               | 1 / 29 (3.45%)<br>1 | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Eye disorders                                                             |                     |                     |                     |
| Diplopia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 29 (3.45%)<br>1 | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Eye Haemorrhage<br>subjects affected / exposed<br>occurrences (all)       | 0 / 29 (0.00%)<br>0 | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Eye Pain<br>subjects affected / exposed<br>occurrences (all)              | 1 / 29 (3.45%)<br>1 | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Photophobia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 29 (0.00%)<br>0 | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Vision Blurred<br>subjects affected / exposed<br>occurrences (all)        | 0 / 29 (0.00%)<br>0 | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Visual Acuity Reduced<br>subjects affected / exposed<br>occurrences (all) | 1 / 29 (3.45%)<br>1 | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Gastrointestinal disorders                                                |                     |                     |                     |
| Abdominal Discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 29 (0.00%)<br>0 | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Breath Odour<br>subjects affected / exposed<br>occurrences (all)          | 0 / 29 (0.00%)<br>0 | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all)  | 0 / 29 (0.00%)<br>0 | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)          | 0 / 29 (0.00%)<br>0 | 1 / 31 (3.23%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Diarrhoea                                                                 |                     |                     |                     |

|                                        |                |                |                 |
|----------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 2 / 29 (6.90%)  |
| occurrences (all)                      | 1              | 0              | 2               |
| Dry Mouth                              |                |                |                 |
| subjects affected / exposed            | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                      | 0              | 0              | 1               |
| Dyspepsia                              |                |                |                 |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                      | 1              | 0              | 1               |
| Flatulence                             |                |                |                 |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0               |
| Gastrooesophageal Reflux Disease       |                |                |                 |
| subjects affected / exposed            | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0               |
| Gingival Bleeding                      |                |                |                 |
| subjects affected / exposed            | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                      | 0              | 0              | 1               |
| Gingival Swelling                      |                |                |                 |
| subjects affected / exposed            | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%)  |
| occurrences (all)                      | 0              | 0              | 1               |
| Haemorrhoids                           |                |                |                 |
| subjects affected / exposed            | 0 / 29 (0.00%) | 1 / 31 (3.23%) | 0 / 29 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0               |
| Nausea                                 |                |                |                 |
| subjects affected / exposed            | 2 / 29 (6.90%) | 1 / 31 (3.23%) | 4 / 29 (13.79%) |
| occurrences (all)                      | 2              | 2              | 4               |
| Oral Discomfort                        |                |                |                 |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0               |
| Umbilical Hernia                       |                |                |                 |
| subjects affected / exposed            | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0               |
| Vomiting                               |                |                |                 |
| subjects affected / exposed            | 1 / 29 (3.45%) | 1 / 31 (3.23%) | 2 / 29 (6.90%)  |
| occurrences (all)                      | 1              | 1              | 2               |
| Skin and subcutaneous tissue disorders |                |                |                 |

|                                                 |                |                |                |
|-------------------------------------------------|----------------|----------------|----------------|
| Alopecia                                        |                |                |                |
| subjects affected / exposed                     | 1 / 29 (3.45%) | 2 / 31 (6.45%) | 0 / 29 (0.00%) |
| occurrences (all)                               | 1              | 2              | 0              |
| Granuloma Annulare                              |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Pain of Skin                                    |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Hypoaesthesia Facial                            |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                               | 0              | 0              | 3              |
| Rash                                            |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Endocrine disorders                             |                |                |                |
| Hypothyroidism                                  |                |                |                |
| subjects affected / exposed                     | 0 / 29 (0.00%) | 0 / 31 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 2 / 29 (6.90%) | 1 / 31 (3.23%) | 1 / 29 (3.45%) |
| occurrences (all)                               | 2              | 1              | 1              |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 2 / 29 (6.90%) | 1 / 31 (3.23%) | 0 / 29 (0.00%) |
| occurrences (all)                               | 2              | 1              | 0              |
| Mobility Decreased                              |                |                |                |
| subjects affected / exposed                     | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Muscular Weakness                               |                |                |                |
| subjects affected / exposed                     | 2 / 29 (6.90%) | 0 / 31 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all)                               | 3              | 0              | 0              |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 1 / 29 (3.45%) | 0 / 31 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all)                               | 1              | 0              | 3              |
| Myalgia                                         |                |                |                |

|                                                                                       |                      |                     |                     |
|---------------------------------------------------------------------------------------|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                      | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0 | 2 / 29 (6.90%)<br>2 |
| Pain in Extremity<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 29 (3.45%)<br>1  | 1 / 31 (3.23%)<br>1 | 1 / 29 (3.45%)<br>1 |
| Infections and infestations                                                           |                      |                     |                     |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 29 (3.45%)<br>2  | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Cellulitis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 29 (0.00%)<br>0  | 1 / 31 (3.23%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Ear Infection<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 29 (3.45%)<br>1  | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Genitourinary Tract Infection<br>subjects affected / exposed<br>occurrences (all)     | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |
| Herpes Simplex<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 29 (3.45%)<br>1  | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                         | 3 / 29 (10.34%)<br>3 | 1 / 31 (3.23%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 29 (3.45%)<br>2  | 3 / 31 (9.68%)<br>3 | 2 / 29 (6.90%)<br>2 |
| Skin Infection<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 29 (0.00%)<br>0  | 1 / 31 (3.23%)<br>1 | 0 / 29 (0.00%)<br>0 |
| Tooth Abscess<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 29 (3.45%)<br>1  | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0 |
| Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1 |

|                                                                                             |                      |                     |                      |
|---------------------------------------------------------------------------------------------|----------------------|---------------------|----------------------|
| Urinary Tract Infection<br>subjects affected / exposed<br>occurrences (all)                 | 3 / 29 (10.34%)<br>3 | 1 / 31 (3.23%)<br>1 | 0 / 29 (0.00%)<br>0  |
| Viral Infection<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 29 (3.45%)<br>1  | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |
| Viral Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 29 (3.45%)<br>6  | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |
| Metabolism and nutrition disorders                                                          |                      |                     |                      |
| Anorexia<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 29 (0.00%)<br>0  | 0 / 31 (0.00%)<br>0 | 3 / 29 (10.34%)<br>3 |
| Decreased Appetite<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 29 (3.45%)<br>1  | 0 / 31 (0.00%)<br>0 | 1 / 29 (3.45%)<br>1  |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 29 (0.00%)<br>0  | 1 / 31 (3.23%)<br>1 | 0 / 29 (0.00%)<br>0  |
| Increased Appetite<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 29 (3.45%)<br>1  | 0 / 31 (0.00%)<br>0 | 0 / 29 (0.00%)<br>0  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 21 October 2008 | The following changes were made in Amendment INT-1: increased CRS target dosage from 400 to 800 mg/day and dosage range changed from 300 to 400 mg/day to 400 to 1,200 mg/day; revised CRS titration schedule to 400 mg/day starting at Week 1 and 800 mg/day starting at Week 2; changed open-label carisbamate (CRS) dosages from 200 to 400 mg/day to 400 to 1,200 mg/day; increased the maximum allowable dosages of each comparator group (TPM: from 300 to 400 mg/day, LEV: from 2,000 to 3,000 mg/day) to be consistent with their respective prescribing information; removed provision that allowed one dosage adjustment during the double-blind maintenance period to reduce unpredictability that may be associated with a change in study drug dosage and to allow better interpretation of the retention rates in the maintenance period, clarified procedures for the double-blind titration period, double-blind maintenance phase, transition phase, double-blind exit phase, and open-label phase, revised objectives, hypothesis, inclusion and exclusion criteria, computerized cognitive test battery, statistical methods, and pharmacogenomics , added/updated algorithms for monitoring liver function tests and for ECG monitoring of the QT interval corrected for heart rate using Fridericia formula (QTcF) interval. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date            | Interruption                                                                                                             | Restart date |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|--------------|
| 20 January 2010 | Carisbamate partial onset seizures studies lacked consistent efficacy data so trials in this indication were terminated. | -            |

Notes:

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

With limitations of low enrollment of subjects per treatment arm and early termination of the study by the sponsor, primary efficacy analysis was not performed and the focus of this report was safety. Safety data should be interpreted cautiously.

Notes: