



Clinical trial results:

A MULTICENTER, OPEN-LABEL, LONG-TERM EXTENSION STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF LACOSAMIDE AS ADJUNCTIVE THERAPY IN PEDIATRIC SUBJECTS WITH EPILEPSY WITH PARTIAL-ONSET SEIZURES

Summary

| | |
|--------------------------|--|
| EudraCT number | 2012-005012-26 |
| Trial protocol | BE IT CZ SK HU ES EE PL GB LV RO BG LT Outside EU/EEA SE |
| Global end of trial date | 13 April 2022 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 16 October 2022 |
| First version publication date | 16 October 2022 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | EP0034 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01964560 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UCB BIOSCIENCES Inc. |
| Sponsor organisation address | 8010 Arco Corporate Drive, Raleigh, United States, NC 27617 |
| Public contact | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |
| Scientific contact | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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 | 14 May 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 13 April 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 13 April 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and tolerability of lacosamide in pediatric subjects

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

1 to 3 concomitant antiepileptic drugs (AEDs) as permitted in the protocol

Evidence for comparator:

Not applicable

| | |
|---|----------------|
| Actual start date of recruitment | 13 August 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Argentina: 9 |
| Country: Number of subjects enrolled | Australia: 6 |
| Country: Number of subjects enrolled | Belgium: 5 |
| Country: Number of subjects enrolled | Brazil: 6 |
| Country: Number of subjects enrolled | Bulgaria: 1 |
| Country: Number of subjects enrolled | China: 14 |
| Country: Number of subjects enrolled | Colombia: 1 |
| Country: Number of subjects enrolled | Croatia: 20 |
| Country: Number of subjects enrolled | Czechia: 9 |
| Country: Number of subjects enrolled | Estonia: 3 |
| Country: Number of subjects enrolled | France: 4 |
| Country: Number of subjects enrolled | Georgia: 47 |
| Country: Number of subjects enrolled | Greece: 2 |
| Country: Number of subjects enrolled | Hungary: 51 |
| Country: Number of subjects enrolled | Israel: 8 |
| Country: Number of subjects enrolled | Italy: 13 |
| Country: Number of subjects enrolled | Latvia: 12 |
| Country: Number of subjects enrolled | Lithuania: 4 |
| Country: Number of subjects enrolled | Mexico: 36 |
| Country: Number of subjects enrolled | Montenegro: 2 |

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Poland: 33 |
| Country: Number of subjects enrolled | Portugal: 1 |
| Country: Number of subjects enrolled | Korea, Republic of: 17 |
| Country: Number of subjects enrolled | Moldova, Republic of: 2 |
| Country: Number of subjects enrolled | Philippines: 2 |
| Country: Number of subjects enrolled | Romania: 24 |
| Country: Number of subjects enrolled | Russian Federation: 29 |
| Country: Number of subjects enrolled | Serbia: 19 |
| Country: Number of subjects enrolled | Slovakia: 14 |
| Country: Number of subjects enrolled | Slovenia: 3 |
| Country: Number of subjects enrolled | Taiwan: 16 |
| Country: Number of subjects enrolled | Thailand: 34 |
| Country: Number of subjects enrolled | Ukraine: 74 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | United States: 17 |
| Worldwide total number of subjects | 540 |
| EEA total number of subjects | 199 |

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) | 103 |
| Children (2-11 years) | 287 |
| Adolescents (12-17 years) | 150 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in August 2014 and concluded in April 2022.

Pre-assignment

Screening details:

The Participant Flow refers to the Safety Set (SS). The SS included all enrolled study participants who took at least 1 dose of lacosamide (LCM) in this long-term extension study.

Period 1

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

Arms

| | |
|-----------|---------------------------|
| Arm title | Lacosamide (All subjects) |
|-----------|---------------------------|

Arm description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing ≥30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing ≥50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Lacosamide |
| Investigational medicinal product code | LCM |
| Other name | VIMPAT |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received LCM administered orally at pre-defined timepoints.

| | |
|--|--------------------|
| Investigational medicinal product name | Lacosamide |
| Investigational medicinal product code | LCM |
| Other name | VIMPAT |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received LCM administered orally at pre-defined timepoints.

| Number of subjects in period 1 | Lacosamide (All subjects) |
|--------------------------------|---------------------------|
| Started | 540 |
| Completed | 395 |
| Not completed | 145 |
| Consent withdrawn by subject | 64 |
| Adverse event, non-fatal | 23 |

| | |
|--|----|
| Surgery-hemispherotomy | 1 |
| Protocol deviation | 2 |
| Patient and Investigator choice | 1 |
| Participant moved to another country | 1 |
| Seizures appeared resolved with epilepsy surgery | 1 |
| Patient was prescribed CBD | 1 |
| Lost to follow-up | 4 |
| Surgery | 1 |
| Lack of efficacy | 46 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Lacosamide (All subjects) |
|-----------------------|---------------------------|

Reporting group description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing ≥30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing ≥50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

| Reporting group values | Lacosamide (All subjects) | Total | |
|--|---------------------------|-------|--|
| Number of subjects | 540 | 540 | |
| Age Categorical Units: participants | | | |
| ≥28 days - <24 months | 103 | 103 | |
| ≥24 months - <12 years | 287 | 287 | |
| ≥12 - <18 years | 150 | 150 | |
| Age Continuous Units: years | | | |
| arithmetic mean | 7.486 | | |
| standard deviation | ± 5.415 | - | |
| Sex: Female, Male Units: participants | | | |
| Female | 236 | 236 | |
| Male | 304 | 304 | |

End points

End points reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Lacosamide (All subjects) |
|-----------------------|---------------------------|

Reporting group description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing ≥30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing ≥50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

Primary: Percentage of participants with treatment-emergent adverse events (TEAEs)

| | |
|-----------------|--|
| End point title | Percentage of participants with treatment-emergent adverse events (TEAEs) ^[1] |
|-----------------|--|

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. Treatment-emergent is defined as starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose. The Safety Set (SS) included all enrolled study participants who took at least 1 dose of LCM in this long-term extension study.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values | Lacosamide (All subjects) | | | |
|-----------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 540 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 77.2 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with serious TEAEs

| | |
|-----------------|--|
| End point title | Percentage of participants with serious TEAEs ^[2] |
|-----------------|--|

End point description:

A serious adverse event (SAE) must meet 1 or more of the following criteria: • Death, • Life-threatening (Life-threatening does not include a reaction that might have caused death had it occurred in a more severe form.), • Significant or persistent disability/incapacity, • Congenital anomaly/birth defect

(including that occurring in a fetus), • Important medical event that, based upon appropriate medical judgment, may jeopardize the patient or participant and may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious., • Initial inpatient hospitalization or prolongation of hospitalization. Treatment-emergent is defined as starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose. The SS included all enrolled study participants who took at least 1 dose of LCM in this long-term extension study.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

Notes:

[2] - 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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values | Lacosamide (All subjects) | | | |
|-----------------------------------|------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 540 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 20.6 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with TEAEs leading to study discontinuation

| | |
|-----------------|---|
| End point title | Percentage of participants with TEAEs leading to study discontinuation ^[3] |
|-----------------|---|

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. AEs leading to study discontinuation. Treatment-emergent is defined as starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose. The SS included all enrolled study participants who took at least 1 dose of LCM in this long-term extension study. Here, only those participants who discontinued the study due to TEAEs starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose of LCM are reported.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

Notes:

[3] - 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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

| End point values | Lacosamide (All subjects) | | | |
|-----------------------------------|------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 540 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 4.1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of seizure-free days during the study

| | |
|-----------------|--|
| End point title | Percentage of seizure-free days during the study |
|-----------------|--|

End point description:

The number of seizure-free days was the total number of days within an interval for which daily diary data were available and no seizures were reported. The percentage of seizure-free days was computed as 100 times the number of seizure-free days in the interval divided by the number of days in the interval for which daily diary data were available. Percentage of seizure-free days was measured using data obtained from participant diaries from EP0034 and is presented for the overall Treatment only. The Full Analysis Set (FAS) was used for the analysis of seizure data and included all study participants in the SS who had at least 1 completed post-Baseline seizure diary. Study participants whose efficacy data could not be source verified were excluded from the FAS. Here, Number of participants analyzed included those participants who were evaluable for the assessment.

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

End point timeframe:

From Week 0 to End of Treatment (up to Week 96)

| | | | | |
|--|------------------------------|--|--|--|
| End point values | Lacosamide (All subjects) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 537 | | | |
| Units: percentage of seizure free days | | | | |
| arithmetic mean (standard deviation) | 66.96 (± 36.18) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

Adverse event reporting additional description:

TEAEs were events which started on or after date of first EP0034 dose of LCM, or whose intensity worsened on or after date of first EP0034 dose of LCM. AEs occurring within 30 days after last dose of LCM were considered treatment-emergent. SS included all enrolled study participants who took at least 1 dose of LCM in the long-term extension study.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Lacosamide (All subjects) |
|-----------------------|---------------------------|

Reporting group description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing ≥30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing ≥50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

| Serious adverse events | Lacosamide (All subjects) | | |
|---|---------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 111 / 540 (20.56%) | | |
| number of deaths (all causes) | 7 | | |
| number of deaths resulting from adverse events | 0 | | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Brain operation | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 540 (0.74%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device malfunction | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cyst | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Device breakage | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device occlusion | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory distress | | | |
| subjects affected / exposed | 3 / 540 (0.56%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| Respiratory failure | | | | |
| subjects affected / exposed | 3 / 540 (0.56%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 2 | | | |
| Pneumonia aspiration | | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Apnoea | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchospasm | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chylothorax | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epistaxis | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypoventilation | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypoxia | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Disorientation | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Emotional disorder of childhood | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Blood bicarbonate decreased | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Liver function test abnormal | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urine output decreased | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Clavicle fracture | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Head injury | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lip injury | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural fistula | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tooth fracture | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Toxicity to various agents | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Cerebral palsy | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Talipes | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Nervous system disorders | | | |
| Convulsion | | | |
| subjects affected / exposed | 24 / 540 (4.44%) | | |
| occurrences causally related to treatment / all | 1 / 30 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Status epilepticus | | | |
| subjects affected / exposed | 9 / 540 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 11 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Epilepsy | | | |
| subjects affected / exposed | 7 / 540 (1.30%) | | |
| occurrences causally related to treatment / all | 1 / 10 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| Partial seizures | | | | |
| subjects affected / exposed | 4 / 540 (0.74%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dizziness | | | | |
| subjects affected / exposed | 3 / 540 (0.56%) | | | |
| occurrences causally related to treatment / all | 1 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Partial seizures with secondary generalisation | | | | |
| subjects affected / exposed | 3 / 540 (0.56%) | | | |
| occurrences causally related to treatment / all | 0 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile convulsion | | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hemiparesis | | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Somnolence | | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Altered state of consciousness | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cognitive disorder | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Grand mal convulsion | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotonia | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intracranial haematoma | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Motor dysfunction | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myoclonic epilepsy | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subdural hygroma | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonic convulsion | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Idiopathic thrombocytopenic purpura | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diplopia | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Parophthalmia | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 10 / 540 (1.85%) | | |
| occurrences causally related to treatment / all | 1 / 12 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nausea | | | |
| subjects affected / exposed | 4 / 540 (0.74%) | | |
| occurrences causally related to treatment / all | 2 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspepsia | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dysphagia | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal motility disorder | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gingival bleeding | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Stomatitis | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Pyuria | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vesicoureteric reflux | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle haemorrhage | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 11 / 540 (2.04%) | | |
| occurrences causally related to treatment / all | 0 / 14 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 5 / 540 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 540 (0.74%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 3 / 540 (0.56%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dengue fever | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Influenza | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rhinovirus infection | | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abscess neck | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute tonsillitis | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adenovirus infection | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Amoebic dysentery | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchiolitis | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Corona virus infection | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related sepsis | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea infectious | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ear infection | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterovirus infection | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis rotavirus | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal infection | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Helicobacter infection | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nasopharyngitis | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oral herpes | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Otitis media | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Otitis media acute | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Periorbital cellulitis | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pharyngotonsillitis | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia influenzal | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Pneumonia pneumococcal | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia respiratory syncytial viral | | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia viral | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 540 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acetonaemia | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Decreased appetite | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enteral feeding intolerance | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypophagia | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 1 / 540 (0.19%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Lacosamide (All subjects) | | |
|---|---------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 289 / 540 (53.52%) | | |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 30 / 540 (5.56%) | | |
| occurrences (all) | 42 | | |
| Headache | | | |
| subjects affected / exposed | 29 / 540 (5.37%) | | |
| occurrences (all) | 89 | | |
| Convulsion | | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed occurrences (all) | 27 / 540 (5.00%) 33 | | |
| General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) | 86 / 540 (15.93%) 149 | | |
| Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) | 56 / 540 (10.37%) 113 42 / 540 (7.78%) 54 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 38 / 540 (7.04%) 49 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) | 83 / 540 (15.37%) 167 57 / 540 (10.56%) 92 39 / 540 (7.22%) 68 33 / 540 (6.11%) 46 28 / 540 (5.19%) 35 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 30 June 2015 | <p>Protocol Amendment 1, dated 30 Jun 2015, provided the following key changes. Based on the date of the amendment, 63 study participants were screened (enrolled into EP0034) prior to this amendment (Table 1.5).</p> <p>The primary purpose of this substantial amendment was to add further clarification regarding the addition of extra procedures electrocardiograms (ECGs) in case of LCM dose increases to ≥ 8 mg/kg/day and ≥ 400 mg/day or in case of addition of new concomitant antiepileptic drugs (AEDs), in accordance with the Food and Drug Administration (FDA) request and based on program specific guidelines. Furthermore, at the request of the Spanish Independent Ethics Committee (IEC), additional inclusion criteria (Inclusion Criterion #5 and #6) were added to clarify age and diagnosis requirements for enrollment.</p> <p>Additional changes were implemented for consistency with other protocols in the LCM pediatric program and administrative changes including the update of the study team and minor corrections, and update of the Sponsor Declaration for electronic signature, were made.</p> |
| 24 March 2017 | <p>Protocol Amendment 2, dated 24 Mar 2017, provided the following key changes. Based on the date of the amendment, 362 study participants were screened (enrolled into EP0034) prior to this amendment (Table 1.5).</p> <p>The primary purpose of this substantial amendment was to allow administration of the Pediatric Quality of Life Inventory (PedsQL) to study participants under 2 years of age and to implement language regarding potential drug-induced liver injury (PDILI) events, based on new standard language which was applied across all protocols at UCB. Addition of this language was to align with FDA guidance regarding monitoring of potential drug-induced liver injury (PDILI) events and did not reflect a change in the liver safety signal for LCM.</p> <p>Permitted and prohibited concomitant medications were also updated and language clarified; neuroleptics (except for clozapine) were allowed during the study and cannabidiols (not approved or indicated for epilepsy by local health authority) were prohibited during the study.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported