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Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Vimpat

Lacosamide

Procedure no: EMEA/H/C/000863/P46/051

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step[1]	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	22 September 2025	17 September 2025
☐	CHMP comments	6 October 2025	25 September 2025
☐	Updated CHMP Rapporteur AR	9 October 2025	N/A
☒	CHMP outcome	16 October 2025	16 October 2025

Administrative information

Procedure resources	
Rapporteur	**Filip Josephson**

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1. Introduction

On 4 August 2025, the MAH submitted a completed paediatric study for Vimpat, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

These data are also submitted as part of the post-authorisation measure(s).

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that EP0151 is a standalone study.

2.2. Information on the pharmaceutical formulation used in the study

Lacosamide oral solution was used in the EP0151 study.

2.3. Clinical aspects

2.3.1. Introduction

Lacosamide has proven to be an effective and safe adjunctive treatment for partial-onset seizures (POS) with or without secondary generalization, based on 3 double-blind, placebo-controlled, multicentre studies (SP667, SP754, and SP755) in study participants with difficult-to-control POS. Lacosamide has also been shown to be an effective and safe adjunctive treatment over the long term for study participants with POS.

Lacosamide has been approved as monotherapy and adjunctive treatment in patients with POS, (minimum age varying between 1 month and 18 years, depending on individual country) and as adjunctive treatment in patients with primary generalized tonic-clonic seizures and in patients with idiopathic generalized epilepsy (minimum age of 4 years, depending on individual country).

In EU Vimpat® (lacosamide) is indicated

- as adjunctive therapy in the treatment of POS with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.

- as monotherapy in the treatment of POS with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.

- as adjunctive treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy.

2.3.2. Clinical study

EP0151

Description

Study EP0151 was an open-label extension follow-up study designed to assess the long-term use of lacosamide oral solution (2mg/kg/day to 12mg/kg/day) in paediatric study participants with epilepsy. The patients were <6 years of age at entry into EP0151 and had completed previous studies with lacosamide (EP0034 or SP848). Treatment with lacosamide oral solution was continued until either the participant reached 6 years of age or until marketing application approval was achieved for paediatric patients in the region of participation and lacosamide oral solution was available (whichever was earliest), unless an exception was granted by the Sponsor.

Methods

Study participants

Participants at entry EP0151 were children with epilepsy <6 years of age who had completed EP0034 or SP848. Study EP0151 was conducted in Georgia, Hungary, Moldova, Romania, Taiwan, and Ukraine.

EP0034 was an open-label study to obtain long-term safety and efficacy data in pediatric subjects (aged 1 month to ≤17 years) with epilepsy with partial-onset seizures treated with LCM oral solution or LCM tablets as adjunctive therapy.

SP848 was an open-label study to evaluate long-term safety, tolerability, and efficacy in children with epilepsy (partial onset seizures) treated with Lacosamide oral solution (syrup). Study SP848 included pediatric patients previously completed clinical Lacosamide trials as well as pediatric patients with epilepsy with partial-onset seizures who had not participated in clinical studies previously.

Assessor's comment:

As depicted in Table 5-2 children were 2 to <6 years old at inclusion in study EP0151. The children were divided in 2 groups ≥ 2 to <4 years (n=19) and ≥4 to < 6 years (n=29).

When included in the previous studies EP0034 or SP848 the children were >2 months to < 4 years. As a result of the design the children were continuously exposed to lacosamide over an extended period.

Table 5-2 modified by the assessor

Age (years) at entry into previous studies, EP0034 or SP848		
Mean (SD)	0.943(0,495)	3.198 (0654)
Median	0.750	3.500
Min, max	0.17, 1.83	2.03, 3,96
Age (years) at entry into EP0151		
Variable	≥ 2 to <4 years	≥4 to < 6 years
N	19	29
Mean (SD)	2.888(0.518)	5.180(0.642)
Median	2.750	5.417
Min, max	2.16, 3.83	4.03, 5.97

Treatment

Lacosamide oral solution (10mg/ml). Minimum dose of 2mg/kg/day to maximum dose of 12mg/kg/day or 600mg/day, whichever was lower, administered BID in the morning and evening.

Concomitant AED was permitted.

Objective

To assess the long-term use of lacosamide oral solution dosed at 2mg/kg/day to 12mg/kg/day when administered to pediatric study participants with epilepsy who have completed EP0034 or SP848.

Outcomes/endpoints

Primary Endpoints:

- TEAEs reported by the study participant or caregiver or observed by the Investigator.
- Withdrawals from study due to TEAEs
- Withdrawals from study due to SAEs
- Modal daily dose (mg/kg/day)
- Maximum daily dose (mg/kg/day)

Based on safety data from clinical studies with lacosamide and general safety considerations, additional TEAEs were given special consideration. These TEAEs were termed other significant TEAEs and included cardiac and electrocardiogram-related terms, suicidality-related terms, abnormal behavior, appetite disorder, decreased appetite, diet refusal, food aversion, hypophagia, loss of consciousness, and syncope.

Sample size

No formal sample size calculations have been performed for this study, as there are no statistical hypotheses being tested. The sample size will be determined by the number of participants in EP0034 or SP848 who have been treated with LCM that are eligible to enter this open-label follow-up study. Approximately 80 to 100 study participants are estimated to be eligible for enrollment.

Randomisation and blinding (masking)

Not applicable.

Statistical Methods

No statistical hypotheses testing was conducted in this study. Descriptive statistics was used to provide an overview of the study results.

Assessor's comment:

The presentation of the study is acknowledged.

Approximately 80-100 children from two previous open label studies were estimated to be eligible for enrollment in the current study to assess the long-term use of lacosamide oral solution in children with POS. Primary endpoints focus on TEAEs and dosage used.

Results

Participant flow

A total of 48 study participants were screened and enrolled at 15 sites in Georgia, Hungary, Moldova, Romania, Taiwan, and Ukraine. All screened study participants were included in the safety set, which included 19 study participants aged ≥2 to <4 years and 29 study participants aged ≥4 to <6 years.

A total of 11 study participants (22.9%) discontinued from the study, including 7 study participants (36.8%) in the ≥2 to <4 years age group and 4 study participants (13.8%) in the ≥4 to <6 years age group. The most common reason for discontinuation was "other" (6 study participants), followed by withdrawal by study participant (2 study participants). Of the 6 study participants with a primary reason for discontinuation of "other", 5 study participants had a discontinuation reason related to the Sponsor's decision to close the study.

Table 5-1: Summary of study participant disposition and discontinuation reasons by age group (SS)

Disposition	≥2 to <4 years N=19 n (%)	≥4 to <6 years N=29 n (%)	All study participants N=48 n (%)
Started study	19 (100)	29 (100)	48 (100)
Treated <12 months	0	5 (17.2)	5 (10.4)
Treated ≥12 months and <24 months	1 (5.3)	4 (13.8)	5 (10.4)
Treated ≥24 months and <36 months	4 (21.1)	4 (13.8)	8 (16.7)
Treated ≥36 months and <48 months	10 (52.6)	12 (41.4)	22 (45.8)
Treated ≥48 months	4 (21.1)	4 (13.8)	8 (16.7)
Completed study	12 (63.2)	25 (86.2)	37 (77.1)
Discontinued	7 (36.8)	4 (13.8)	11 (22.9)
Primary reason for discontinuation			
Adverse event	0	2 (6.9)	2 (4.2)
Lack of efficacy	0	0	0
Protocol deviation	0	0	0
Lost to follow up	1 (5.3)	0	1 (2.1)
Withdrawal by study participant	1 (5.3)	1 (3.4)	2 (4.2)
Other	5 (26.3)	1 (3.4)	6 (12.5)

CSR=clinical study report; eCRF=electronic Case Report Form; SS=Safety Set
Note: Completed study was defined as study participants who had "Study Termination (Completed Subject)" selected as status at termination.
Note: A month was defined as 28 days.
Note: Age group was defined by age at time of entry into EP0151.
Note: "Withdrawal by study participant" was reported as "Consent withdrawn (not due to adverse event)" in the eCRF.
Note: Approval to provide lacosamide oral solution was granted on a case-by-case basis in certain participants ≥6 years of age who needed a longer period of treatment with lacosamide oral solution.
Data source: EP0151 final CSR Table 1.4

Recruitment

Children with epilepsy <6 years of age who had completed EP0034 or SP848 were recruited. A total of 48 study participants were screened and enrolled.

Baseline data

Table 5-2: Study participant demographics by age group (SS)

Variable	≥2 to <4 years N=19	≥4 to <6 years N=29	All study participants N=48
Age at entry into first pediatric study (years)			
n	19	29	48
Mean (SD)	0.943 (0.495)	3.198 (0.654)	2.305 (1.261)
Median	0.750	3.500	2.420
Min, max	0.17, 1.83	2.03, 3.96	0.17, 3.96
Age at entry into EP0151 (years)			
n	19	29	48
Mean (SD)	2.888 (0.518)	5.180 (0.642)	4.273 (1.277)
Median	2.750	5.417	4.390
Min, max	2.16, 3.83	4.03, 5.97	2.16, 5.97
Gender, n (%)			
Male	13 (68.4)	20 (69.0)	33 (68.8)
Female	6 (31.6)	9 (31.0)	15 (31.3)
Weight at Baseline (kg)			
n	19	29	48
Mean (SD)	8.01 (1.85)	13.16 (2.86)	11.12 (3.56)
Median	7.30	14.00	10.35
Min, max	4.8, 12.3	7.0, 17.3	4.8, 17.3
Weight at Visit 1 of EP0151 (kg)			
n	19	29	48
Mean (SD)	12.58 (2.33)	16.40 (4.06)	14.89 (3.93)
Median	12.30	16.10	14.45
Min, max	9.5, 18.9	8.0, 24.3	8.0, 24.3
Height at Baseline (cm)			
n	19	29	48
Mean (SD)	71.18 (7.66)	94.25 (8.99)	85.12 (14.16)
Median	74.00	95.00	85.00
Min, max	57.0, 83.0	74.0, 110.0	57.0, 110.0

Table 5-2: Study participant demographics by age group (SS)

Variable	≥2 to <4 years N=19	≥4 to <6 years N=29	All study participants N=48
Height at Visit 1 of EP0151 (cm)			
n	19	29	48
Mean (SD)	89.34 (5.41)	104.79 (10.48)	98.68 (11.62)
Median	90.00	108.00	96.25
Min, max	80.0, 100.0	84.0, 120.0	80.0, 120.0
BMI at Baseline (kg/m^2)			
n	19	29	48
Mean (SD)	15.69 (1.82)	14.76 (2.39)	15.13 (2.21)
Median	15.79	14.28	15.17
Min, max	11.8, 19.2	8.4, 18.4	8.4, 19.2
BMI at Visit 1 of EP0151 (kg/m^2)			
n	19	29	48
Mean (SD)	15.796 (2.847)	14.807 (2.527)	15.198 (2.673)
Median	15.300	14.900	15.230
Min, max	12.40, 24.40	10.40, 18.90	10.40, 24.40
Country			
Georgia	≤10	≤10	≤10
Hungary	≤10	≤10	12 (25.0)
Moldova	0	≤10	≤10
Romania	0	≤10	≤10
Taiwan	≤10	≤10	≤10
Ukraine	≤10	12 (41.4)	22 (45.8)
Racial group, n (%)			
American Indian/Alaskan Native	0	0	0
Asian	≤10	≤10	≤10
Black	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
White	18 (94.7)	28 (96.6)	46 (95.8)
Other/Mixed	0	0	0
Ethnicity, n (%)			
Hispanic/Latino	0	≤10	≤10

Table 5-2: Study participant demographics by age group (SS)

Variable	≥2 to <4 years N=19	≥4 to <6 years N=29	All study participants N=48
Not Hispanic/Latino	19 (100)	26 (89.7)	45 (93.8)

BMI=body mass index; CSR=clinical study report; SS=Safety Set
Note: Percentages were based on the number of study participants in the SS.
Note: Baseline was defined as the last non-missing value collected prior to the first dose of lacosamide in the first lacosamide study.
Data sources: EP0151 final CSR Table 2.1 and EP0151 final CSR Table 9.1

Number analysed

In total 48 patients participated in the study. Nineteen patients were aged ≥2 to < 4 years and 29 patients aged ≥ 4 to < 6 years.

Efficacy results

Not applicable.

Safety results

Exposure

The 19 study participants aged ≥2 to <4 years were exposed to lacosamide for a minimum of 573 days and a maximum of 1406 days with the majority of these participants being exposed for up to 48 months in this study.

The 29 study participants aged ≥4 to <6 years of age were exposed to lacosamide for a minimum of 1 day and a maximum of 1501 days with the majority of these participants being exposed for up to 42 months.

AE

In EP0151, 19 study participants (39.6%) experienced 81 **TEAE**s while being treated with lacosamide. TEAEs were most common in the SOCs of *Infections and infestations* (13 study participants), Gastrointestinal disorders (5 study participants), *General disorders* and administration site conditions (5 study participants), and *Respiratory, thoracic, and mediastinal disorders* (5 study participants). No TEAEs were considered related to lacosamide by the Investigator.

Overall, 7 study participants (14.6%) experienced 20 **serious TEAEs**. The most frequently reported SOCs among all study participants were *Infections and infestations* (4 study participants), followed by *General disorders and administration site conditions* and *Nervous system disorders* (2 study participants each). No serious TEAEs by PT were reported for more than 1 study participant.

A total of 2 study participants died during the study. No deaths were considered related to lacosamide by the Investigator.

No study participants experienced **other significant TEAEs** during the study.

The safety observations in EP0151 were consistent with the known safety profile of lacosamide. Observations in EP0151 were as expected for the pediatric population and no new safety concerns were identified.

Table 5-3: Incidence of serious TEAEs by age group (SS)

MedDRA v16.1 SOC PT	≥2 to <4 years N=19 n (%) [#]	≥4 to <6 years N=29 n (%) [#]	All study participants N=48 n (%) [#]
Any serious TEAEs	2 (10.5) [4]	5 (17.2) [16]	7 (14.6) [20]
Cardiac disorders	0	1 (3.4) [1]	1 (2.1) [1]
Cardiac failure acute	0	1 (3.4) [1]	1 (2.1) [1]
Congenital, familial and genetic disorders	0	1 (3.4) [1]	1 (2.1) [1]
Developmental hip dysplasia	0	1 (3.4) [1]	1 (2.1) [1]
General disorders and administration site conditions	0	2 (6.9) [8]	2 (4.2) [8]
Device malfunction	0	1 (3.4) [7]	1 (2.1) [7]
Sudden death	0	1 (3.4) [1]	1 (2.1) [1]
Infections and infestations	1 (10.5) [3]	2 (6.9) [3]	4 (8.3) [6]
Bronchopneumonia	1 (5.3) [1]	0	1 (2.1) [1]
Pneumonia	1 (5.3) [1]	0	1 (2.1) [1]
Pneumonia necrotising	0	1 (3.4) [1]	1 (2.1) [1]
Rhinovirus infection	0	1 (3.4) [1]	1 (2.1) [1]
Septic shock	1 (5.3) [1]	0	1 (2.1) [1]
Viral infection	0	1 (3.4) [1]	1 (2.1) [1]
Nervous system disorders	1 (5.3) [1]	1 (3.4) [2]	2 (4.2) [3]
Epilepsy	1 (5.3) [1]	0	1 (2.1) [1]
Partial seizures with secondary generalization	0	1 (3.4) [2]	1 (2.1) [2]
Respiratory, thoracic and mediastinal disorders	0	1 (3.4) [1]	1 (2.1) [1]
Acute respiratory failure	0	1 (3.4) [1]	1 (2.1) [1]

CSR=clinical study report; MedDRA=Medical Dictionary for Regulatory Activities; PT=preferred term; SOC=system organ class; SS=Safety Set; TEAE=treatment-emergent adverse event
Note: n is the number of study participants reporting at least 1 serious TEAE within the SOC/PT.
Note: [#] is the number of individual occurrences of the serious TEAE.
Note: Percentages were based on the number of study participants in the SS.
Data source: EP0151 final CSR Table 8.2.2

2.3.3. Discussion on clinical aspects

Assessors comment

The MAH has submitted a completed paediatric study for Vimpat, in accordance with Article 46 of Regulation (EC) No1901/2006.

Study EP0151 was an open-label, long-terms follow- up safety study to assess the long-term use of lacosamide oral solution. A total of 48 participants with epilepsy aged ≥2 to < 6 years at entry into EP0151 were included. The number was significantly lower than what was estimated (80-100). All patients had previously completed EP0034 or SP848 and received lacosamide treatment in those studies.

The majority of the participants aged ≥2 to <4 years (n=19) were exposed to lacosamide for up to 48 months in the study and the majority of the study participants aged ≥4 to <6 years (n=29) were exposed to lacosamide for up to 42 months. The median daily dose in both age groups was 10 mg/ kg and the median maximum daily dose was 10 mg/kg (range 4-12 mg/kg). In EU the maximum recommended dose in *monotherapy* in children from 2 years of age is up to 12 mg/kg/day in patients ≥ 10kg to < 40kg. In *adjunctive* therapy the maximum recommended dose is up to 12mg/kg/day in patients ≥10kg to < 20 kg and 10 mg/kg/day in patients ≥20kg to < 30 kg. Accordingly, the doses administered in the study were consistent with the SmPC.

Eleven participants discontinued the study. None of them due to lack of efficacy. Nineteen study participants (39.6%) experienced 81 TEAEs while being treated with lacosamide. No TEAEs were considered related to lacosamide by the Investigator. A total of 2 study participants died during the study. No deaths were considered related to lacosamide by the Investigator.

To summarise 48 children (aged ≥2 to <6 years at study entry) were exposed to lacosamide oral solution up to 48 months. The doses used in the study were in line with the recommended doses in EU. Lacosamide was well-tolerated and no new safety concerns were identified.

The study had no efficacy endpoint.

No changes to the approved EU Summary of Product Information for Vimpat are proposed following the results of study EP0151.

3. Rapporteur's CHMP overall conclusion and recommendation

The obligation to submit paediatric data collected in study EP0151 in accordance with Article 46 of Regulation (EC) No1901/2006 is fulfilled. No changes to the approved EU Summary of Product Information for Vimpat are being proposed following the completion of study EP0151.

☒ **Fulfilled:**

No regulatory action required.