EMA/512497/2023

European Medicines Agency decision

P/0470/2023

of 1 December 2023

on the refusal of a modification of an agreed paediatric investigation plan for lacosamide (Vimpat), (EMEA-000402-PIP03-17-M08) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0153/2017 issued on 2 June 2017, the decision P/0336/2017 issued on 30 October 2017, the decision P/0048/2018 issued on 22 February 2018, the decision P/0059/2019 issued on 28 February 2019, the decision P/0330/2020 issued on 21 August 2020, the decision P/0349/2021 issued on 20 August 2021, and the decision P/0247/2022 issued on 8 July 2022,

Having regard to the application submitted by UCB Pharma S.A. on 2 August 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 October 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the refusal of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the refusal of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for lacosamide (Vimpat), syrup, film-coated tablet, oral use; solution for infusion, intravenous use, including changes to the deferral, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, are hereby refused.

Article 2

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0132/2013 issued on 31 May 2013, including subsequent modifications thereof.

Article 3

This decision is addressed to UCB Pharma S.A., Allée de la Recherche 60, 1070 – Brussels, Belgium.

EMA/PDCO/440776/2023
Amsterdam, 13 October 2023

Opinion of the Paediatric Committee on the refusal of a modification of an agreed Paediatric Investigation Plan

EMEA-000402-PIP03-17-M08

Scope of the application

Active substance(s):

Lacosamide

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of generalized epilepsy and epilepsy syndromes

Pharmaceutical form(s):

Syrup

Solution for infusion

Film-coated tablet

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

UCB Pharma S.A.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, UCB Pharma S.A. submitted to the European Medicines Agency on 2 August 2023 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0153/2017 issued on 2 June 2017, the decision P/0336/2017 issued on 30 October 2017, the decision P/0048/2018 issued on 22 February 2018, the decision P/0059/2019 issued on

28 February 2019, the decision P/0330/2020 issued on 21 August 2020, the decision P/0349/2021 issued on 20 August 2021, and the decision P/0247/2022 issued on 8 July 2022.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 11 September 2023.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends, as set out in the appended summary report:

   - to refuse the changes proposed by the applicant regarding the paediatric investigation plan and the deferral.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

Not applicable

2. Paediatric Investigation Plan

2.1. Condition

Treatment of generalised epilepsy and epileptic syndromes

2.1.1. Indication(s) targeted by the PIP

Treatment of generalised epilepsy and epileptic syndromes

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Solution for infusion

Syrup

2.1.4. Measures

Area	Description
Quality-related studies	**Measure 1** Confirmation of the age-appropriateness of the current commercial lacosamide film-coated tablets (for oral use) for the target population. **Measure 2** Confirmation of the age-appropriateness of the current commercial lacosamide solution for infusion (for intravenous use) for the target population. **Measure 3** Confirmation of the age-appropriateness of the current commercial lacosamide syrup (for oral use) for the target population.
Clinical studies	**Study 12** Open-label, multicentre study to investigate the pharmacokinetics (PK) of lacosamide (commercially available tablet or oral solution) as therapy in children (aged from 1 month to less than 18 years) who are prescribed lacosamide for epilepsy (SP1047).

	Study 14 Exploratory, open-label, study in paediatric subjects from 1 month to less than 18 years for safety and tolerability and preliminary efficacy for adjunctive lacosamide treatment of epilepsy syndromes associated with generalised seizures excluding primary generalised tonic clonic seizures with Idiopathic Generalised Epilepsy and excluding typical absence (Type IIA1) or atypical absence (Type IIA2) seizures when occurring exclusively from other seizure types (SP0966). **Study 15** Open-label, multi-centre, parallel-group, non-inferiority efficacy, safety, tolerability and PK study for adjunctive lacosamide treatment in neonates with repeated electroencephalographic neonatal seizures (SP0968). *Study 17: deleted during procedure EMEA-000402-PIP03-17-M03.* **Study 18** Open label, long term safety, tolerability and pharmacokinetic study in children from 1 month to less than 18 years with epilepsy; extension study for subjects from other LCM studies including SP847 and SP0966 (SP848). **Study 20** Double-blind, randomised, placebo-controlled, parallel group, multi-centre study to evaluate efficacy and safety of lacosamide as adjunctive treatment for uncontrolled primary generalised tonic-clonic (PGTC) seizures in subjects aged 4 years and above with idiopathic generalized epilepsy (IGE) (SP0982). **Study 21** Open-label, multi-centre, extension study to evaluate safety and tolerability of lacosamide as adjunctive treatment for idiopathic generalised epilepsy (IGE) with uncontrolled primary generalized tonic-clonic (PGTC) seizures in subjects aged 4 years and above with idiopathic generalised epilepsy (IGE) (EP0012).

Extrapolation, modelling and simulation studies	**Study 4** PBPK prediction of oral lacosamide pharmacokinetics and dose adaptations in children from birth to less than 18 years (CL0096). **Study 5** Population pharmacokinetics of lacosamide in children with partial onset seizures aged from 1 month to less than 18 years, based in data from studies SP847 and SP1047. **Study 6** Physiologically based pharmacokinetic (PBPK) prediction of intravenous lacosamide pharmacokinetics and dose adaptations in neonates (aged from birth to 28 days). **Study 7** Predictive population pharmacokinetics of intravenous lacosamide in children from birth to less than 18 years. **Study 8** Final retrospective population pharmacokinetics model of lacosamide in children from birth to less than 18 years, combining all available data at the end of the program.
Other studies	Not applicable
Other measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of epilepsy with partial-onset seizures.

   Authorised indication(s):

   - Vimpat is indicated as monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy.

Authorised pharmaceutical form(s):

Film-coated tablet

Syrup

Solution for infusion

Authorised route(s) of administration:

Oral use

Intravenous use