EMA/533642/2015

European Medicines Agency decision

P/0183/2015

of 17 August 2015

on the acceptance of a modification of an agreed paediatric investigation plan for lacosamide (Vimpat) (EMEA-000402-PIP02-11-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This Decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0132/2013 issued on 31 May 2013 and the decision P/0275/2014 issued on 28 October 2014,

Having regard to the application submitted by UCB Pharma S.A. on 27 April 2015 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 17 July 2015, 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 acceptance of changes to the agreed paediatric investigation plan.

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

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

Has adopted this decision:

Article 1

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

Article 2

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

Done at London, 17 August 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/303549/2015
London, 17 July 2015

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

EMEA-000402-PIP02-11-M02

Scope of the application

Active substance(s):

Lacosamide

Invented name:

Vimpat

Condition(s):

Treatment of epilepsy with partial onset seizures

Treatment of generalised epilepsy and epileptic syndromes

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Syrup

Solution for infusion

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

UCB Pharma S.A.

Information about the authorised medicinal product:

See Annex II

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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 27 April 2015 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0132/2013 issued on 31 May 2013 and the decision P/0275/2014 issued on 28 October 2014.

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

The procedure started on 19 May 2015.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

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 agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

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 epilepsy with partial onset seizures

2.1.1. Indication(s) targeted by the PIP

Treatment of epilepsy with partial onset seizures.

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

Syrup

Solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality - related studies	3	**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	7	**Study 11** Open-label safety and pharmacokinetic adjunctive treatment study in paediatric subjects from 1 month to less than 18 years of age with partial-onset seizures (SP847). **Study 12**

Area	Number of measures	Description
		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 13** Double blind, randomised, parallel group, placebo controlled adjunctive treatment study of lacosamide in children with partial-onset seizures aged from 1 month to less than 4 years to evaluate safety, tolerability and pharmacokinetics (SP0967). **Study 15** Open-label, multi-centre, parallel-group, non-inferiority efficacy, safety and tolerability study for adjunctive lacosamide treatment of neonatal seizures in term neonates (SP0968). **Study 16** Open-label, active controlled study comparing the safety of lacosamide as monotherapy in children from 1 month to less than 18 years of age with partial-onset seizures with or without secondarily generalized seizures (SP0XXX). **Study 18** Open label, long term safety, tolerability and pharmacokinetic study in children from birth to less than 18 years with epilepsy; extension study for subjects from SP847, SP0966, and SP0968 (SP848). **Study 19** Open-label long-term extension study in children from 1 month to less than 18 years with partial-onset seizures to evaluate safety, tolerability, effects on behaviour, cognition and quality of life (EP0034).
Extrapolation, modelling and simulation studies	7	**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**

Area	Number of measures	Description
		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. **Study 9** Exposure-response modelling of oral lacosamide in adjunctive treatment of children with POS, using the data from the Phase 3 studies SP0967 (1 month to less than 4 years of age) and SP0969 (4 years to less than 18 years). **Study 10** Bridging PK and PK/PD simulations to determine paediatric dose adaptation rules for POS monotherapy with lacosamide in children aged 1 month to less than 18 years.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition: treatment of generalised epilepsy and epileptic syndromes

2.2.1. Indication(s) targeted by the PIP

Treatment of generalised epilepsy and epileptic syndromes.

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

From birth to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Solution for infusion

Syrup

2.2.4. Measures

Area	Number of measures	Description

Area	Number of measures	Description
Quality - related studies	3	**Measure 1** As described for condition 'Treatment of epilepsy with partial onset seizures'. **Measure 2** As described for condition 'Treatment of epilepsy with partial onset seizures'. **Measure 3** As described for condition 'Treatment of epilepsy with partial onset seizures'.
Clinical studies	7	**Study 12** As described for condition 'Treatment of epilepsy with partial onset seizures'. **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 generalized epilepsy excluding primary generalised tonic clonic seizures with Idiopathic Generalised Epilepsy (SP0966). **Study 15** As described for condition 'Treatment of epilepsy with partial onset seizures'. **Study 17** Double-blind, randomized, placebo-controlled study in children from 1 month to less than 18 years with generalized epilepsy excluding primary generalised tonic clonic seizures with idiopathic generalised epilepsy (syndrome to be determined based on results of SP0966) (SP0YYY). **Study 18** As described for condition 'Treatment of epilepsy with partial onset seizures'. **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 generalized 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 generalized epilepsy (IGE) with uncontrolled primary generalized tonic-clonic (PGTC) seizures in subjects aged 4 years and above with idiopathic generalized epilepsy (IGE) (EP0012).

Area	Number of measures	Description
Extrapolation, modelling and simulation studies	5	**Study 4** As described for condition 'Treatment of epilepsy with partial onset seizures'. **Study 5** As described for condition 'Treatment of epilepsy with partial onset seizures'. **Study 6** As described for condition 'Treatment of epilepsy with partial onset seizures'. **Study 7** As described for condition 'Treatment of epilepsy with partial onset seizures'. **Study 8** As described for condition 'Treatment of epilepsy with partial onset seizures'.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2022
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 adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent (16-18 years) patients with epilepsy.

Authorised pharmaceutical form(s):

Film-coated tablet, syrup, solution for infusion.

Authorised route(s) of administration:

Oral use, intravenous use.