EMA/127868/2020

European Medicines Agency decision

P/0120/2020

of 18 March 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral for cenobamate (EMEA-002563-PIP02-19) 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 application submitted by Arvelle Therapeutics Netherlands B.V. on 15 July 2019 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 28 February 2020, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for cenobamate, tablet, film-coated tablet, age-appropriate oral liquid dosage form, age-appropriate dosage form for parenteral use, oral use, parenteral use, gastric use, 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, is hereby agreed.

Article 2

A deferral for cenobamate, tablet, film-coated tablet, age-appropriate oral liquid dosage form, age-appropriate dosage form for parenteral use, oral use, parenteral use, gastric use, 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, is hereby granted.

Article 3

This decision is addressed to Arvelle Therapeutics Netherlands B.V., Johannes Vermeerplein 9, 1071 DV – Amsterdam, Netherlands.

EMA/PDCO/684403/2019 Corr
Amsterdam, 28 February 2020

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral

EMEA-002563-PIP02-19

Scope of the application

Active substance(s):

Cenobamate

Condition(s):

Treatment of epilepsy

Pharmaceutical form(s):

Tablet

Film-coated tablet

Age-appropriate oral liquid dosage form

Age-appropriate dosage form for parenteral use

Route(s) of administration:

Oral use

Parenteral use

Gastric use

Name/corporate name of the PIP applicant:

Arvelle Therapeutics Netherlands B.V.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Arvelle Netherlands B.V. submitted for agreement to the European Medicines Agency on 15 July 2019 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 20 August 2019.

Supplementary information was provided by the applicant on 29 November 2019. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

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

2. The measures and timelines of the agreed paediatric investigation plan 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 annex 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

2.1.1. Indication(s) targeted by the PIP

Treatment of epilepsy

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)

Tablet

Film-coated tablet

Age-appropriate oral liquid dosage form

Age-appropriate dosage form for parenteral use

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an oral liquid solution with minimum loading of 10 mg/ml. (CMC0X1) **Study 2** Development of a parenteral formulation with appropriate dose load, volume, dispensing accuracy and excipients that are suitable for the neonatal population. (CMC0X2)
Non-clinical studies	1	**Study 3** Non-clinical study to evaluate the local tolerance of the intravascular and perivascular administration of the parenteral formulation. (NC0X1)

Area	Number of measures	Description
Clinical studies	7	**Study 4** Open-label study to evaluate pharmacokinetics, safety and exploratory efficacy of cenobamate as adjunctive therapy in the paediatric population from 2 to less than 18 years of age with epilepsy with focal onset seizures. (C0X1) **Study 5** Open-label study to evaluate pharmacokinetics, safety and exploratory efficacy of cenobamate as adjunctive therapy in the paediatric population from 1 month to less than 2 years of age with epilepsy with focal onset seizures. (C0X2) **Study 6** Randomised, double-blind, placebo-controlled study to evaluate the efficacy, safety, and tolerability of cenobamate as adjunctive therapy in the paediatric population from 1 month to less than 4 years of age with epilepsy with focal onset seizures. (C0X3) **Study 7** Open-label study to evaluate pharmacokinetics, safety and efficacy of cenobamate in the paediatric population from 2 years to less than 18 years of age with a range of paediatric epilepsy syndromes with generalized seizures. (C0X5) **Study 8** Randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of cenobamate in the paediatric population from 1 month to less than 18 years of age with a specified epilepsy syndrome as determined by the results from Study C0X5. (C0X6) **Study 9** Study to evaluate pharmacokinetics (open-label phase), safety and efficacy (double-blind phase) of cenobamate in the paediatric population from birth to less than 1 month of age with epilepsy with refractory seizures (C0X8) **Study 10** Long-term open-label study to evaluate safety of cenobamate in the paediatric population that completed studies C0X1, C0X2, C0X3, C0X5, C0X6 and C0X8 (C0X9)

Area	Number of measures	Description
Extrapolation, modelling and simulation studies	5	**Study 11** PopPK study to confirm or modify the paediatric posology compared to the regimen used in study C0X1. PopPK study to predict initial paediatric doses to be used in studies C0X2 and C0X5 (MS1) **Study 12** PopPK study to confirm or modify the paediatric posology compared to the regimen used in study C0X2. PopPK study to predict initial paediatric doses to be used in studies C0X8 and paediatric doses to be used in study C0X3 (MS2) **Study 13** PopPK study to confirm or modify the paediatric posology compared to the regimen used in study C0X8 (MS4) **Study 14** PopPK study to confirm or modify the paediatric posology compared to the regimen used in study C0X5 (MS5) **Study 15** Extrapolation study for paediatric patients from 4 to less than 12 years of age with epilepsy with focal-onset seizures (MS3)
Other studies	0	Not applicable.
Other measures	0	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 October 2029
Deferral for one or more measures contained in the paediatric investigation plan:	Yes