EMA/386634/2021

European Medicines Agency decision

P/0300/2021

of 13 August 2021

on the acceptance of a modification of an agreed paediatric investigation plan for cenobamate (ONTOZRY), (EMEA-002563-PIP02-19-M01) 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/0120/2020 issued on 18 March 2020,

Having regard to the application submitted by A.C.R.A.F. SpA on 19 March 2021 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 25 June 2021, 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 and to the deferral.

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

Changes to the agreed paediatric investigation plan for cenobamate (ONTOZRY), tablet, film-coated tablet, age-appropriate oral liquid dosage form, age-appropriate dosage form for parenteral use, oral use, parenteral use, gastric use, including changes to the deferral, 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 A.C.R.A.F. SpA, 70 Viale Amelia, 00181 – Rome, Italy.

EMA/PDCO/183715/2021 corr
Amsterdam, 25 June 2021

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

EMEA-002563-PIP02-19-M01

Scope of the application

Active substance(s):

Cenobamate

Invented name:

ONTOZRY

Condition(s):

Treatment of epilepsy

Authorised indication(s):

See Annex II

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:

A.C.R.A.F. SpA

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, A.C.R.A.F. SpA submitted to the European Medicines Agency on 19 March 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0120/2020 issued on 18 March 2020.

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

The procedure started on 27 April 2021.

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 and to the deferral 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 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

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 suspension 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)
Clinical studies	7	**Study 4** Open-label study consisting of two linked clinical protocols (C0X39/C0X40) to evaluate the 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. (C0X39/C0X40) **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)
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 May 2030.
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

Authorised indication(s):

- Adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite a history of treatment with at least 2 anti-epileptic medicinal products.

Authorised pharmaceutical form(s):

Tablet

Film-coated tablet

Authorised route(s) of administration:

Oral use