EMA/631062/2022

European Medicines Agency decision

P/0351/2022

of 11 August 2022

on the acceptance of a modification of an agreed paediatric investigation plan for bempedoic acid (Nilemdo), (EMEA-001872-PIP01-15-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 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/0094/2017 issued on 11 April 2017 and the decision P/0185/2018 issued on 17 July 2018,

Having regard to the application submitted by Esperion Therapeutics, Inc. on 21 March 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 June 2022, 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, 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 bempedoic acid (Nilemdo), film-coated tablet, age-appropriate oral liquid dosage form, age-appropriate oral solid dosage form, oral 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 Esperion Therapeutics, Inc., 3891 Ranchero Drive, Suite 150, 48108 - Ann Arbor, MI, United States.

EMA/PDCO/193890/2022
Amsterdam, 24 June 2022

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

EMEA-001872-PIP01-15-M02

Scope of the application

Active substance(s):

Bempedoic acid

Invented name:

Nilemdo

Condition(s):

Treatment of elevated cholesterol

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral liquid dosage form

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Esperion Therapeutics, Inc.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Esperion Therapeutics, Inc. submitted to the European Medicines Agency on 21 March 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0094/2017 issued on 11 April 2017 and the decision P/0185/2018 issued on 17 July 2018.

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

The procedure started on 25 April 2022.

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 Paediatric Committee member of Norway 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

1.1. Condition:

Treatment of elevated cholesterol

The waiver applies to:

- the paediatric population from birth to less than 4 years;
- film-coated tablet, age-appropriate formulation, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of elevated cholesterol

2.1.1. Indication(s) targeted by the PIP

Treatment of heterozygous and homozygous familial hypercholesterolemia

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

From 4 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate formulation

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1:** Development of an age-appropriate formulation.
Non-clinical	**Study 2:** Dose range-finding juvenile rat toxicity study to evaluate potential adverse effects of bempedoic acid on developing organ systems in juvenile rats beginning on PND 15 until adulthood, and to determine the relevant dose(s) for the definitive juvenile rat study.

	Study 3: Definitive juvenile rat toxicity study to evaluate potential toxicity of bempedoic acid on developing organ systems in juvenile rats from PND 15 (prepubertal) through sexual maturity to support administration of bempedoic acid to children of at least 4 years of age.
Clinical	**Study 4:** Open-label, un-controlled, dose escalating PK/PD study to evaluate the dose and exposure/response relationship, safety and tolerability of bempedoic acid when added to stable background lipid modifying therapy in patients from 6 to less than 18 years of age with heterozygous familial hypercholesterolaemia.(1002-041). **Study 5:** Double-blind, placebo-controlled, parallel-group, efficacy and safety study to evaluate the effect of bempedoic acid versus placebo when added to baseline lipid-modifying therapy on percent change from baseline to Week 12 in LDL-C in patients from 6 to less than 18 years of age with heterozygous familial hypercholesterolaemia. (1002-042). **Study 6:** Open-label, un-controlled, PK/PD, safety and activity study to evaluate the dose and exposure/response relationship, tolerability, safety and activity of bempedoic acid when added to stable background lipid modifying therapy in patients from 4 to less than 18 years of age with homozygous and compound heterozygous familial hypercholesterolaemia (HoFH and CHeFH). (1002-051).
Extrapolation, modelling and simulation studies	Not applicable
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:	No
Date of completion of the paediatric investigation plan:	By September 2027
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 elevated cholesterol

Authorised indication(s):

- Nilemdo is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
  - in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
  - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use