EMA/627382/2020

European Medicines Agency decision

P/0475/2020

of 1 December 2020

on the acceptance of a modification of an agreed paediatric investigation plan for fenfluramine (hydrochloride), (EMEA-001990-PIP01-16-M03) 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/0251/2017 issued on 8 September 2017 and the decision P/0177/2018 issued on 15 June 2018 and the decision P/0354/2018 issued on 30 November 2018,

Having regard to the application submitted by Zogenix International Ltd on 13 July 2020 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 16 October 2020, 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 fenfluramine (hydrochloride), oral solution, oral use, gastric 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 Zogenix International Ltd., The Pearce Building, West Street, Maidenhead, Berkshire, SL6 1RL – Maidenhead, United Kingdom.

EMA/PDCO/399298/2020
Amsterdam, 16 October 2020

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

EMEA-001990-PIP01-16-M03

Scope of the application

Active substance(s):

Fenfluramine (hydrochloride)

Condition(s):

Treatment of Dravet syndrome

Pharmaceutical form(s):

Oral solution

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Zogenix International Ltd

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Zogenix International Ltd submitted to the European Medicines Agency on 13 July 2020 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/0251/2017 issued on 8 September 2017 and the decision P/0177/2018 issued on 15 June 2018 and the decision P/0354/2018 issued on 30 November 2018.

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

The procedure started on 18 August 2020.

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 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)

Waiver

1.1. Condition:

Treatment of Dravet syndrome

The waiver applies to:

- all subsets of the paediatric population from birth to less than 1 year of age;
- oral solution, oral use, gastric use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of Dravet syndrome

2.1.1. Indication(s) targeted by the PIP

The adjunctive treatment of seizures in patients with Dravet syndrome

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

From 1 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Oral solution

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Acceptability/palatability report **Study 2** Development of an age-appropriate oral solution and strength
Non-clinical studies	2	**Study 3** Dose range-finding juvenile toxicity study (9000468) **Study 4** Definitive juvenile toxicity study (9000406)

Clinical studies	4	**Study 5** Multicentre, randomised, double-blind, placebo-controlled, parallel group trial of two fixed doses of fenfluramine as an adjunctive therapy in children and young adults from 2 to less than 18 years of age with Dravet Syndrome (ZX008-Study 1) **Study 6** Multicentre, randomised, double-blind, placebo-controlled, parallel group trial of two fixed doses of fenfluramine as an adjunctive therapy in children and young adults from 2 to less than 18 years of age with Dravet Syndrome (ZX008-Study2) **Study 7** Open-label extension trial to assess the long-term safety of fenfluramine (ZX008-1503) **Study 8** 2-cohort trial to first assess the PK and safety profile of a single dose of fenfluramine when added to standard of care, followed by a randomised, double-blind, placebo-controlled, parallel group evaluation of the efficacy, safety and tolerability of fenfluramine as adjunctive therapy to stiripentol treatment in children and young adults from 2 to less than 18 years of age with Dravet Syndrome (ZX008-1504)
Extrapolation, modelling and simulation studies	0	**Study 9 deleted** during procedure EMEA-001990-PIP01-16-M03
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:	No
Date of completion of the paediatric investigation plan:	By June 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes