EMA/503514/2017

European Medicines Agency decision

P/0251/2017

of 8 September 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for fenfluramine (hydrochloride) (EMEA-001990-PIP01-16) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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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 Zogenix International Ltd on 28 November 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 July 2017, in accordance with Article 18 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 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 and on the granting of a waiver.

(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.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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 fenfluramine (hydrochloride), oral solution, oral 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 fenfluramine (hydrochloride), oral solution, oral 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

A waiver for fenfluramine (hydrochloride), oral solution, oral 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 4

This decision is addressed to Zogenix International Ltd, Siena Court, Broadway, SL6 1NJ – Maidenhead, United Kingdom.

EMA/PDCO/305592/2017
London, 21 July 2017

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

EMEA-001990-PIP01-16

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 16(1) of Regulation (EC) No 1901/2006 as amended, Zogenix International Ltd submitted for agreement to the European Medicines Agency on 28 November 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 3 January 2017.

Supplementary information was provided by the applicant on 28 April 2017. 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 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 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)

1. 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 for oral use and 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	1	**Study 9** Modelling and simulation study to evaluate the use of fenfluramine in children from 1 to less than 18 years of age with Dravet syndrome
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