

EMA/677648/2022

## European Medicines Agency decision P/0390/2022

of 9 September 2022

on the acceptance of a modification of an agreed paediatric investigation plan for fenfluramine (hydrochloride) (Fintepla), (EMA-001990-PIP01-16-M05) 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.**

# European Medicines Agency decision

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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<sup>1</sup>,

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<sup>2</sup>,

Having regard to the European Medicines Agency's decision P/0251/2017 issued on 8 September 2017, the decision P/0177/2018 issued on 15 June 2018, the decision P/0354/2018 issued on 30 November 2018, the decision P/0475/2020 issued on 1 December 2020 and the decision P/0502/2021 issued on 2 December 2021,

Having regard to the application submitted by Zogenix International Ltd on 25 April 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 22 July 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.
- (2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1, as amended.

<sup>2</sup> OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

**Article 1**

Changes to the agreed paediatric investigation plan for fenfluramine (hydrochloride) (Fintepla), 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.



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/PDCO/241283/2022  
Amsterdam, 22 July 2022

## Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-001990-PIP01-16-M05

### Scope of the application

**Active substance(s):**

Fenfluramine (hydrochloride)

**Invented name:**

Fintepla

**Condition(s):**

Treatment of Dravet syndrome

**Authorised indication(s):**

See Annex II

**Pharmaceutical form(s):**

Oral solution

**Route(s) of administration:**

Oral use

Gastric use

**Name/corporate name of the PIP applicant:**

Zogenix International Ltd

**Information about the authorised medicinal product:**

See Annex II



## **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 25 April 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/0251/2017 issued on 8 September 2017, the decision P/0177/2018 issued on 15 June 2018, the decision P/0354/2018 issued on 30 November 2018, the decision P/0475/2020 issued on 1 December 2020 and the decision P/0502/2021 issued on 2 December 2021.

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

The procedure started on 23 May 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 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 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

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 year to less than 18 years of age

### 2.1.3. Pharmaceutical form(s)

Oral solution

### 2.1.4. Measures

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

Clinical studies	<p><b>Study 5</b></p> <p>Randomised, double-blind, placebo-controlled, parallel group trial of two fixed doses of fenfluramine as adjunctive therapy in paediatric patients from 2 years to less than 18 years of age with Dravet syndrome (ZX008-Study 1)</p> <p><b>Study 6</b></p> <p>Randomised, double-blind, placebo-controlled, parallel group trial of two fixed doses of fenfluramine as adjunctive therapy in paediatric patients from 2 years to less than 18 years of age with Dravet syndrome (ZX008-Study 2)</p> <p><b>Study 7</b></p> <p>Open-label extension trial to assess the long-term safety of fenfluramine (ZX008-1503)</p> <p><b>Study 8</b></p> <p>2-cohort trial to first assess the pharmacokinetics 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 paediatric patients from 2 years to less than 18 years of age with Dravet syndrome (ZX008-1504)</p> <p><b>Study 10</b></p> <p>Open-label, single-arm trial to assess safety, tolerability and pharmacokinetics of fenfluramine in patients from 1 year to less than 2 years of age with Dravet syndrome (ZX008-2201). <i>This study was added as a result of procedure EMEA-001990-PIP01-16-M04.</i></p>
Extrapolation, modelling and simulation studies	<p><b>Study 9</b></p> <p><i>This study was deleted as a result of procedure EMEA-001990-PIP01-16-M03.</i></p>
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 March 2025
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 Dravet syndrome

Authorised indication(s):

- Treatment of seizures associated with Dravet syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older.

**Authorised pharmaceutical form(s):**

Oral solution

**Authorised route(s) of administration:**

Oral use