EMADOC-1700519818-2034841

European Medicines Agency decision

EMA/PE/0000233398

of 14 April 2025

on the acceptance of a modification of an agreed paediatric investigation plan for fenfluramine hydrochloride (Fintepla) 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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on the acceptance of a modification of an agreed paediatric investigation plan for fenfluramine hydrochloride (Fintepla) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/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, the decision P/0502/2021 issued on 2 December 2021 and the decision P/0390/2022 issued on 9 September 2022,

Having regard to the application submitted by UCB Pharma on 8 November 2024 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 28 February 2025, 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 fenfluramine hydrochloride (Fintepla), 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 UCB Pharma, Allee De La Recherche 60, 1070 – Anderlecht, Belgium.

EMADOC-1700519818-1811230 Corr[1]
Amsterdam, 28 February 2025

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

EMA/PE/0000233398

Scope of the application

Active substance(s):

Fenfluramine (hydrochloride)

Invented name and authorisation status:

See Annex II

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:

UCB Pharma

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, UCB Pharma submitted to the European Medicines Agency on 8 November 2024 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, the decision P/0502/2021 issued on 2 December 2021 and the decision P/0390/2022 issued on 9 September 2022.

[1] 7 April 2025

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

The procedure started on 2 January 2025.

Scope of the modification

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

Clinical studies	**Study 5** 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). **Study 6** 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). **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 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). **Study 10** 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). *This study was added as a result of procedure EMEA-001990-PIP01-16-M04.*
Extrapolation, modelling and simulation studies	**Study 9** *This study was deleted as a result of procedure EMEA-001990-PIP01-16-M03.*
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 December 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of Dravet syndrome

- Treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older.
  - Invented name(s): Fintepla
  - Authorised pharmaceutical form(s): oral solution
  - Authorised route(s) of administration: oral use
  - Authorised via centralised

2. Treatment of Lennox-Gastaut syndrome

- Treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older.
  - Invented name(s): Fintepla
  - Authorised pharmaceutical form(s): oral solution
  - Authorised route(s) of administration: oral use
  - Authorised via centralised