MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-100462-PIP01-22-M01) and to the deferral

MHRA-100462-PIP01-22-M02

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

Name / Corporate name of the PIP applicant

UCB Pharma Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, UCB Pharma Ltd submitted to the licensing authority on 14/07/2023 11:23 BST an application for a Modification

The procedure started on 09/11/2023 12:24 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100462-PIP01-22-M02

Of 11/12/2023 19:53 GMT

On the adopted decision for FENFLURAMINE HYDROCHLORIDE (MHRA-100462-PIP01-22-M02) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for FENFLURAMINE HYDROCHLORIDE, Oral solution , ORAL USE .

This decision is addressed to UCB Pharma Ltd, 208 Bath Road, Berkshire, UNITED KINGDOM, SL1 3WE

ANNEX I

1. Waiver

1.1 Condition:

Treatment of Dravet syndrome The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Oral solution Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of Dravet syndrome

2.2 Indication(s) targeted by the PIP:

Adjunctive treatment of seizures in patients with Dravet syndrome

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 1 year to less than 18 years of age

2.4 Pharmaceutical Form(s):

Oral solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Acceptability/palatability report. Study 2 Development of an age-appropriate oral solution and strength.
Non-Clinical Studies	2	Study 3 (9000468) Dose range-finding juvenile toxicity study. Study 4 (9000406) Definitive juvenile toxicity study.
Clinical Studies	5	Study 5 (ZX008-Study 1) 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. Study 6 (ZX008-Study 2) 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. Study 7 (ZX008-1503) Open-label extension trial to assess the long-term safety of fenfluramine. Study 8 (ZX008-1504) 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. Study 10 (ZX008-2201) Added during procedure MHRA-100462-PIP01-22-M01 Open-label, single arm trial to assess safety and tolerability and pharmacokinetics of fenfluramine in patients from 1 year to less than 2 years of age with Dravet syndrome.
Extrapolation, Modeling & 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 a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/03/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes