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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral

MHRA-100654-PIP01-22

Scope of the Application

Active Substance(s)

triheptanoin

Condition(s)

Treatment of long-chain fatty acid oxidation disorders (LC-FAOD)

Pharmaceutical Form(s)

Oral liquid

Route(s) of Administration

ORAL USE; ENTERAL USE

Name / Corporate name of the PIP applicant

Ultragenyx Germany GmbH

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Ultragenyx Germany GmbH submitted to the licensing authority on 17/10/2022 13:38 BST an application for a Paediatric Investigation Plan

The procedure started on 25/08/2023 12:04 BST

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 agree a paediatric investigation plan and grant a 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-100654-PIP01-22

Of 30/10/2023 07:46 GMT

On the adopted decision for triheptanoin (MHRA-100654-PIP01-22) 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 a paediatric investigation plan and grant a deferral

This decision applies to a Paediatric Investigation Plan for triheptanoin, Oral liquid , ORAL USE; ENTERAL USE .

This decision is addressed to Ultragenyx Germany GmbH, Rahel-Hirsch-Str. 10, Berlin, GERMANY, 10557

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of long-chain fatty acid oxidation disorders (LC-FAOD)

2.2 Indication(s) targeted by the PIP:

Treatment of long-chain fatty acid oxidation disorders (LC-FAOD)

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

All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Oral liquid

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Stability of Dojolvi (UX007) emulation with feeding tubes (P_0876_41) Study 2 Dojolvi (UX007) In-Use Food Stability Report (VV-10677)
Non-Clinical Studies	2	Study 3 9-Month Oral (Dietary) Toxicity and Toxicokinetic Study of Triheptanoin in Juvenile Yucatan Minipigs (UX007-PC002) Study 4 Pre- and Post-Natal Development (PPND; Segment III) Toxicity study of Triheptanoin in Rats (UX007-PC017)
Clinical Studies	6	Study 5 Prospective, interventional, open-label Phase 2 study to evaluate the impact of triheptanoin on acute clinical pathophysiology associated with long-chain fatty acid oxidation disorders (LC-FAOD). (UX007-CL201) Study 6 Prospective, interventional, open-label, long-term, Phase 2, 3-cohort study to evaluate the long-term safety and efficacy of triheptanoin in subjects with long-chain fatty acid oxidation disorders (LC-FAOD). (UX007-CL202) Study 7 Randomized, double-blind Investigator-initiated Phase 2 study to determine if triheptanoin therapy (an odd-chain fatty acid triglyceride) has a therapeutic advantage over conventional treatment for long-chain fatty acid oxidation disorders. Gillingham et al., 2017 (NCT01379625) Study 8 Retrospective medical

		record review study comparing clinical outcomes before and after triheptanoin initiation in LC-FAOD patients to evaluate the therapeutic benefit and safety of triheptanoin treatment. (UX007-CL001) Study 9 Retrospective chart review study to assess the clinical outcome of triheptanoin treatment in patients with long-chain fatty acid oxidation disorders (LC-FAOD) treated under expanded access program. (UX007-CL003) Study 10 Double-blind, randomised, active-controlled trial to evaluate safety and efficacy of triheptanoin compared to even-chain MCT in children from birth to less than 18 years of age with long-chain fatty acid oxidation disorders. (UX007-CL302)
Extrapolation, Modeling & Simulation Studies	1	Study 11 Population PK Modelling of Heptanoate in Healthy Subjects and Patients with Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD) Administered with Triheptanoin
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:	30/06/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes