MHRA
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Canary Wharf
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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-100178-PIP01-21

Scope of the Application

Active Substance(s)

DTX401 (a nonreplicating, recombinant adeno-associated virus serotype 8 vector that contains a codon-optimized, wild-type human glucose-6-phosphatase (G6PC) gene)

Condition(s)

Treatment of glycogen storage disease type 1a (GSDIa)

Pharmaceutical Form(s)

Concentrate and diluent for solution for infusion

Route(s) of Administration

Intravenous 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 10/09/2021 14:23 BST an application for a Paediatric Investigation Plan

The procedure started on 04/07/2022 11:34 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 and grant a waiver

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-100178-PIP01-21

Of 11/07/2022 16:07 BST

On the adopted decision for DTX401 (a nonreplicating, recombinant adeno-associated virus serotype 8 vector that contains a codon-optimized, wild-type human glucose-6-phosphatase (G6PC) gene) (MHRA-100178-PIP01-21) 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

This decision applies to a Paediatric Investigation Plan for DTX401 (a nonreplicating, recombinant adeno-associated virus serotype 8 vector that contains a codon-optimized, wild-type human glucose-6-phosphatase (G6PC) gene), Concentrate and diluent for solution for infusion , Intravenous use .

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

ANNEX I

1. Waiver

1.1 Condition:

Treatment of glycogen storage disease type 1a (GSDIa) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Concentrate and diluent for solution for infusion Route(s) of administration: Intravenous use Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of glycogen storage disease type 1a (GSDIa)

2.2 Indication(s) targeted by the PIP:

Treatment of glycogen storage disease type 1a (GSDIa)

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

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Concentrate and diluent for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	1	Study 1 (CRL Study number: 20282036) Juvenile animal efficacy study to evaluate the potential loss of vector expression and pharmacological effects at various ages to better inform paediatric dose selection.
Clinical Studies	2	Study 2 (DTX401-CL301) Randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of DTX401 in patients 8 years of age and older with glycogen storage disease type 1a (GSDIa). In particular, the reduction or elimination of dependence on exogenous glucose replacement therapy and the effect of DTX401 on glucose control will be evaluated. Study 3 (DTX401-CL302) Open-label, non-comparative study to determine the efficacy and confirm the safety of DTX401 in paediatric patients with GSDIa aged 2 years to less than 8 years. To evaluate the efficacy of DTX401 in providing normal G6Pase activity, and thereby reducing the need for glucose replacement therapy at night while maintaining or improving glycaemic control.
Extrapolation, Modeling & Simulation Studies	0	Not applicable
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:	Yes
Date of completion of the paediatric investigation plan:	30/06/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes