EMA/359172/2021

European Medicines Agency decision

P/0278/2021

of 8 July 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene (DTX401) (EMEA-002734-PIP01-19) 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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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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Ultragenyx Germany GmbH on 20 December 2019 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 May 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene (DTX401), concentrate and diluent for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene (DTX401), concentrate and diluent for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene (DTX401), concentrate and diluent for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

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

EMA/PDCO/154270/2021
Amsterdam, 21 May 2021

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-002734-PIP01-19

Scope of the application

Active substance(s):

Adeno-associated viral vector serotype 8 containing the human glucose-6-phosphatase gene (DTX401)

Condition(s):

Treatment of glycogen storage disease type Ia

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 opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Ultragenyx Germany GmbH submitted for agreement to the European Medicines Agency on 20 December 2019 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 28 January 2020.

Supplementary information was provided by the applicant on 12 February 2021. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 annex 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

Treatment of glycogen storage disease type Ia

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- concentrate and diluent for solution for infusion, intravenous use;
- 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:

Treatment of glycogen storage disease type Ia

2.1.1. Indication(s) targeted by the PIP

Treatment of glycogen storage disease type Ia

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate and diluent for solution for infusion

2.1.4. Measures

Area	**Number of measures**	**Description**
Quality-related studies	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 Randomized, double-blind, placebo- controlled Phase 3 clinical study to evaluate the efficacy and safety of DTX401 in patients 8 years of age and older with

		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 pediatric patients with GSDIa aged 2 years to <8 years of age to evaluate the efficacy of DTX401 in providing normal G6Pase activity, and thereby reducing the need for glucose replacement therapy at night (eg, enteral nutrition, cornstarch therapy) while maintaining or improving glycemic control
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes