EMA/470006/2023

European Medicines Agency decision

P/0432/2023

of 27 October 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for self-complementary adeno-associated virus [AAV] serotype 8 virus particle encoding the human ornithine transcarbamylase [OTC] gene sequence (DTX301), (EMEA-002830-PIP01-20) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Ultragenyx Germany GmbH on 17 April 2020 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 8 September 2023, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for self-complementary adeno-associated virus [AAV] serotype 8 virus particle encoding the human ornithine transcarbamylase [OTC] gene sequence (DTX301), concentrate 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 self-complementary adeno-associated virus [AAV] serotype 8 virus particle encoding the human ornithine transcarbamylase [OTC] gene sequence (DTX301), concentrate 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 self-complementary adeno-associated virus [AAV] serotype 8 virus particle encoding the human ornithine transcarbamylase [OTC] gene sequence (DTX301), concentrate 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/279904/2023
Amsterdam, 8 September 2023

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

EMEA-002830-PIP01-20

Scope of the application

Active substance(s):

Self-complementary adeno-associated virus [AAV] serotype 8 virus particle encoding the human ornithine transcarbamylase [OTC] gene sequence (DTX301)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of ornithine transcarbamylase deficiency

Pharmaceutical form(s):

Concentrate 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 17 April 2020 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 26 May 2020.

Supplementary information was provided by the applicant on 30 May 2023. 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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   The Paediatric Committee member of Norway 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 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 ornithine transcarbamylase deficiency

The waiver applies to:

- the paediatric population from birth to less than 1 month of age;
- concentrate for solution for infusion, intravenous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Treatment of ornithine transcarbamylase deficiency

2.1.1. Indication(s) targeted by the PIP

Treatment of ornithine transcarbamylase (OTC) deficiency

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

From 1 month to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of a concentrate for solution for infusion suitable for use in the paediatric population.
Non-clinical studies	**Study 2 (20282036, DTX301-21-0001)** Pharmacology study in juvenile Otcspf-ash mice to determine the vector loss (loss in vector genome DNA, mRNA transgene and OTC enzyme activity) and integration following a single DTX301 administration. **Study 3 (20324173)** Definitive juvenile toxicity study to support the evaluation of the use of DTX301 in the paediatric population from 1 month of age.
Clinical studies	**Study 4 (DTX301-CL301)**

	Randomized, double-blind, placebo-controlled study to evaluate safety and efficacy of DTX301 in patients from 12 years to less than 18 years of age (and adults) with late-onset ornithine transcarbamylase (OTC) deficiency. **Study 5 (DTX301-CL302)** Open-label study to determine the activity and confirm the safety of DTX301 in paediatric patients with neonatal-onset and late-onset OTC deficiency from 1 month to less than 12 years of age.
Modelling and simulation studies	Not applicable.
Other studies	Not applicable.
Extrapolation plan	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 October 2030
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:

The product is not authorised anywhere in the European Community.