EMA/37957/2023

European Medicines Agency decision

P/0087/2023

of 10 March 2023

on the acceptance of a modification of an agreed paediatric investigation plan for evinacumab (Evkeeza), (EMEA-002298-PIP01-17-M05) 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 European Medicines Agency's decision P/0404/2018 issued on 20 December 2018, decision P/0105/2020 issued on 18 March 2020, decision P/0069/2021 issued on 17 March 2021, decision P/0514/2021 issued on 3 December 2021, and decision P/0394/2022 issued on 9 September 2022,

Having regard to the application submitted by Ultragenyx Germany GmbH on 17 October 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 20 January 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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

Changes to the agreed paediatric investigation plan for evinacumab (Evkeeza), concentrate for solution for infusion, intravenous use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

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

EMA/PDCO/864180/2022
Amsterdam, 20 January 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-002298-PIP01-17-M05

Scope of the application

Active substance(s):

Evinacumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of elevated cholesterol

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 22 of Regulation (EC) No 1901/2006 as amended, Ultragenyx Germany GmbH submitted to the European Medicines Agency on 17 October 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0404/2018 issued on 20 December 2018, decision P/0105/2020 issued on 18 March 2020, decision P/0069/2021 issued on 17 March 2021, decision P/0514/2021 issued on 3 December 2021, and decision P/0394/2022 issued on 9 September 2022.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 21 November 2022.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the 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 elevated cholesterol

The waiver applies to:

- the paediatric population from birth to less than 5 years of age;
- concentrate for solution for infusion, intravenous use;
- 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:

Treatment of elevated cholesterol

2.1.1. Indication(s) targeted by the PIP

Evinacumab is indicated as an adjunct to diet and other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of patients with homozygous familial hypercholesterolemia (HoFH), including patients with double null/negative low-density lipoprotein-receptor (LDL-R) mutations.

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

From 5 years 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	Not applicable.
Non-clinical studies	**Study 1 (R1500-TX-18035)** Dose range-finding juvenile toxicity study to inform dose selection for Study 2 **Study 2 (REGN1-TX-17093)** A 17-Week Intravenous Study in Juvenile Rabbits with a 31-week Recovery Period

	Study 3 (R1500-TX-17094) Intravenous and Subcutaneous Toxicology Study in Juvenile Rats
Clinical studies	**Study 4 (R1500-CL-1629)** Double-blind, randomised, placebo controlled trial of 24 weeks to evaluate safety and efficacy of Evinacumab as add-on to lipid modifying therapies (LMT) in children from 12 years to less than 18 years of age (and adults) with insufficiently controlled homozygous familial hypercholesterolaemia (HoFH) on stable LMT, followed by a 24 week open label treatment period to evaluate safety and a 24-week follow-up period after the last dose of study drug for those patients who choose not to enter the open-label long term safety study (Study 6) **Study 5 (R1500-CL-17100)** A three-part, single arm, open-label trial to evaluate pharmacokinetics, safety and activity of Evinacumab in children from 5 years to less than 12 years of age with HoFH **Study 6 (R1500-CL-1719)** Open-label, long term trial to evaluate safety and activity of Evinacumab in children from 12 years to less than 18 years of age (and adults) with HoFH following completion of Study 4 or are evinacumab naïve and directly enrolled into this study
Extrapolation, modelling and simulation studies	**Study 7 (R1500-CL-17100-Extrapolation)** Extrapolation study to evaluate the use of Evinacumab in the proposed paediatric indication in children from 5 to less than 12 years of age with HoFH
Other studies	Not applicable
Other measures	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 May 2024
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:

Condition(s) and authorised indication(s):

1. Treatment of elevated cholesterol

Authorised indication(s):

- Evkeeza is indicated as an adjunct to diet and other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and adolescent patients aged 12 years and older with homozygous familial hypercholesterolaemia (HoFH).

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use