EMA/829832/2018

European Medicines Agency decision

P/0404/2018

of 20 December 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for evinacumab (EMEA-002298-PIP01-17) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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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 Regeneron Ireland U.C. on 26 February 2018 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 16 November 2018, 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 evinacumab, 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 evinacumab, 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 evinacumab, 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 Regeneron Ireland U.C., Europa House, Harcourt Centre, Harcourt Street, 2 Dublin, Ireland.

EMA/PDCO/563074/2018 Corr
London, 16 November 2018

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

EMEA-002298-PIP01-17

Scope of the application

Active substance(s):

Evinacumab

Condition(s):

Treatment of elevated cholesterol

Pharmaceutical form(s):

Solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Regeneron Ireland U.C.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Regeneron Ireland U.C. submitted for agreement to the European Medicines Agency on 26 February 2018 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 3 April 2018.

Supplementary information was provided by the applicant on 13 August 2018. The applicant proposed modifications to the paediatric investigation plan.

A meeting with the Paediatric Committee took place on 14 November 2018.

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 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

1.1. Condition:

Treatment of elevated cholesterol

The waiver applies to:

- the paediatric population from birth to less than 5 years of age;
- 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 LDL-C lowering therapies for the treatment of patients with homozygous familial hypercholesterolemia (HoFH), including patients with double null/negative 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)

Solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	3	**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 8-week Recovery Period.

Area	Number of measures	Description
		Study 3 (R1500-TX-17094) Intravenous and Subcutaneous Toxicology Study in Juvenile Rats.
Clinical studies	3	**Study 4 (R1500-CL-1629)** Double-blind, randomised, placebo controlled trial of 24 weeks to evaluate safety and efficacy of Evanicumab 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 (HoHF) 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 two part, single arm, open-label trial to evaluate pharmacokinetics, safety and activity of Evanicumab in children from 5 years to less than 12 years of age with HoHF. **Study 6 (R1500-CL-1719)** Open-label, long term trial to evaluate safety and activity of Evanicumab in children from 5 years to less than 18 years of age with HoHF following completion of Study 4 or 5.
Extrapolation, modelling and simulation studies	1	**Study 7 (R1500-CL-17100-Extrapolation)** Extrapolation study to evaluate the use of Evanicumab in the proposed paediatric indication in children from 5 to less than 12 years of age with HoHF.
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 April 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes