EMA/194970/2018

European Medicines Agency decision

P/0105/2018

of 11 April 2018

on the acceptance of a modification of an agreed paediatric investigation plan for evolocumab (Repatha), (EMEA-001268-PIP01-12-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 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 European Medicines Agency's decision P/0127/2013 issued on 28 May 2013, the decision P/0071/2015 issued on 1 April 2015, the decision P/0070/2016 issued on18 March 2016, the decision P/0235/2016 issued on 9 September 2016 and the decision P/0101/2017 issued on 11 April 2017,

Having regard to the application submitted by Amgen Europe B.V. on 5 December 2017 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 23 February 2018, 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 and to the deferral.

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

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for evolocumab (Repatha), solution for injection, subcutaneous use, including changes to the deferral, 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 Amgen Europe B.V., Minervum 7061, 4817-ZK - Breda, The Netherlands.

EMA/PDCO/830568/2017
London, 23 February 2018

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

EMEA-001268-PIP01-12-M05

Scope of the application

Active substance(s):

Evolocumab

Invented name:

Repatha

Condition(s):

Treatment of elevated cholesterol

Treatment of mixed dyslipidaemia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Amgen Europe B.V.

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Amgen Europe B.V. submitted to the European Medicines Agency on 5 December 2017 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/0127/2013 issued on 28 May 2013, the decision P/0071/2015 issued on 1 April 2015, the decision P/0070/2016 issued on18 March 2016, the decision P/0235/2016 issued on 9 September 2016 and the decision P/0101/2017 issued on 11 April 2017.

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

The procedure started on 3 January 2018.

Scope of the modification

Some timelines 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 and to the deferral in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member 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 10 years;
- solution for injection, subcutaneous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

1.2. Condition

Treatment of mixed dyslipidaemia

The waiver applies to:

- the paediatric population from birth to less than 18 years;
- solution for injection, subcutaneous 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 elevated cholesterol

2.1.1. Indication(s) targeted by the PIP

Treatment of heterozygous and homozygous familial hypercholesterolemia

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

From 10 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of a solution for injection in a pre-filled pen, for subcutaneous use **Study 6** Development of a solution for injection in a pre-filled cartridge, for subcutaneous use
Non-clinical studies	2	**Study 2** Study to assess toxicology of combined rosuvastatin and evolocumab administration compared with rosuvastatin alone in Cynomolgus monkeys during 3 months of dosing and a 4-month recovery period **Study 3** Study to assess maternal toxicity, toxicokinetics, antibody development and prenatal and postnatal development in Cynomolgus monkeys, pregnant females from gestation day 20-22 and their offspring up to 6 months postpartum
Clinical studies	2	**Study 4** Double-blind, randomised, multicentre, placebo-controlled, parallel group study to characterise the efficacy, safety, and tolerability of 24 weeks of evolocumab for LDL-C reduction, as add-on to diet and lipid-lowering therapy, in patients from 10 to less than 18 years of age with heterozygous familial hypercholesterolemia **Study 5** Open-label, single-arm, multicentre study to evaluate the safety, tolerability and activity of evolocumab for LDL-C reduction, as add-on to diet and lipid-lowering therapy, in patients from 10 to less than 18 years of age with heterozygous familial hypercholesterolemia or homozygous familial hypercholesterolemia
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 December 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of elevated cholesterol

Authorised indication(s):

- Repatha is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
  - in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL C goals with the maximum tolerated dose of a statin or,
  - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.
- Repatha is indicated in adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.

The effect of Repatha on cardiovascular morbidity and mortality has not yet been determined.

2. Treatment of mixed dyslipidaemia

Authorised indication(s):

- Repatha is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:
  - in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL C goals with the maximum tolerated dose of a statin or,
  - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

The effect of Repatha on cardiovascular morbidity and mortality has not yet been determined.

Authorised pharmaceutical form(s):

Solution for injection

Authorised route(s) of administration:

Subcutaneous use