EMA/331021/2023

European Medicines Agency decision

P/0322/2023

of 11 August 2023

on the acceptance of a modification of an agreed paediatric investigation plan for inclisiran (sodium) (Leqvio), (EMEA-002214-PIP01-17-M02) 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/0321/2018 issued on 12 September 2018 and the decision P/0495/2022 issued on 2 December 2022,

Having regard to the application submitted by Novartis Europharm Ltd. on 17 March 2023 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 June 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 inclisiran (sodium) (Leqvio), solution for injection, subcutaneous 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 Novartis Europharm Ltd., Vista Building Elm Park Merrion Road, D04 A9N6 - Dublin 4, Ireland.

EMA/PDCO/143753/2023
Amsterdam, 23 June 2023

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

EMEA-002214-PIP01-17-M02

Scope of the application

Active substance(s):

Inclisiran (sodium)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of elevated cholesterol

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Novartis Europharm Ltd.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Ltd. submitted to the European Medicines Agency on 17 March 2023 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/0321/2018 issued on 12 September 2018 and the decision P/0495/2022 issued on 2 December 2022.

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

The procedure started on 24 April 2023.

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 6 years of age;
- 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 familial hypercholesterolemia (HeFH)

Treatment of homozygous familial hypercholesterolemia (HoFH)

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

From 6 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1** Two-stage, randomized study to evaluate the safety, tolerability and efficacy of inclisiran versus placebo, used in combination with other lipid lowering therapy in paediatric subjects with homozygous familial hypercholesterolaemia (HoFH) from 12 years to less than 18 years of age [ORION-13 (CKJX839C12302)].

	Study 2 Two-stage, randomized, study to evaluate the safety, tolerability and efficacy of inclisiran versus placebo, used in combination with other lipid lowering therapy in paediatric patients with heterozygous familial hypercholesterolaemia (HeFH) from 12 years to less than 18 years of age [ORION-16 (CKJX839C12301)]. **Study 3** Two-stage, randomised, controlled versus placebo study to evaluate the safety, tolerability and efficacy of inclisiran, used in combination with other lipid lowering therapy in children with homozygous familial hypercholesterolaemia (HoFH) from 6 years to less than 12 years of age [ORION-19 (CKJX839C12304)]. **Study 4** Two-stage, randomized, study to evaluate the safety, tolerability and efficacy of inclisiran versus placebo, used in combination with other lipid lowering therapy in paediatric patients with heterozygous familial hypercholesterolaemia (HeFH) from 6 years to less than 12 years of age [ORION-20 (CKJX839C12303)].
Extrapolation, modelling and simulation studies	Not applicable
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 June 2028
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):

- Leqvio 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
  - Invented name(s): Leqvio
  - Authorised pharmaceutical form(s): solution for injection (injection)
  - Authorised route(s) of administration: subcutaneous use
  - Authorised via centralised procedure
- Leqvio is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated
  - Invented name(s): Leqvio
  - Authorised pharmaceutical form(s): solution for injection (injection)
  - Authorised route(s) of administration: subcutaneous use
  - Authorised via centralised procedure