EMA/317902/2021

European Medicines Agency decision

P/0239/2021

of 17 June 2021

on the acceptance of a modification of an agreed paediatric investigation plan for ravulizumab (Ultomiris), (EMEA-002077-PIP01-16-M04) 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/0199/2017 issued on 14 July 2017, the decision P/0356/2017 issued on 1 December 2017, the decision P/0166/2019 issued on 15 May 2019 and the decision P/0399/2020 issued on 23 October 2020,

Having regard to the application submitted by Alexion Europe SAS on 12 February 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 May 2021, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for ravulizumab (Ultomiris), concentrate for solution for infusion, solution for injection, intravenous use, 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 Alexion Europe SAS, 103-105 rue Anatole France, 92300 - Levallois-Perret, France.

EMA/PDCO/131977/2021 Corr
Amsterdam, 21 May 2021

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

EMEA-002077-PIP01-16-M04

Scope of the application

Active substance(s):

Ravulizumab

Invented name:

Ultomiris

Condition(s):

Treatment of paroxysmal nocturnal haemoglobinuria

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Solution for injection

Route(s) of administration:

Intravenous use

Subcutaneous use

Name/corporate name of the PIP applicant:

Alexion Europe SAS

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Alexion Europe SAS submitted to the European Medicines Agency on 12 February 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0199/2017 issued on 14 July 2017, the decision P/0356/2017 issued on 1 December 2017, the decision P/0166/2019 issued on 15 May 2019 and the decision P/0399/2020 issued on 23 October 2020.

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

The procedure started on 23 March 2021.

Scope of the modification

Some measures and 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 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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of paroxysmal nocturnal haemoglobinuria (PNH)

2.1.1. Indication(s) targeted by the PIP

Treatment of paroxysmal nocturnal haemoglobinuria

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 5** *(same study as Study 4 in 001943-PIP01-16-M05 and subsequent modifications thereof)* *(This study was added as a result of procedure 002077-PIP01-16-M03.)* Development of an age-appropriate subcutaneous formulation
Non-clinical studies	0	Not applicable
Clinical studies	2	**Study 1 (ALXN1210-PNH-304)** Open-label, multicentre, single arm trial to evaluate pharmacokinetic (PK) and pharmacodynamic (PD) parameters, efficacy and safety of ravulizumab in children less than 18 years of age with PNH **Study 6 (ALXN1210-SC-301)** *(same study as Study 5 in 001943-PIP01-16-M05 and subsequent modifications thereof)*

		(This study was added as a result of procedure 002077-PIP01-16-M03.) Open label multi-centre study to evaluate pharmacokinetics, pharmacodynamics, efficacy and safety of ravulizumab following subcutaneous administration in children from 2 years to less than 18 years of age with atypical haemolytic uraemic syndrome (aHUS) or PNH
Extrapolation, modelling and simulation studies	5	**Study 2** *(same study as Study 3 in 001943-PIP01-16-M05 and subsequent modifications thereof)* Modelling and simulation study to evaluate the use of intravenous ravulizumab in children from birth to less than 18 years of age **Study 3** Extrapolation study to evaluate the efficacy, PK/PD and safety of ravulizumab in paediatric PNH patients from 12 to less than 18 years of age **Study 4** Extrapolation study to evaluate the efficacy, PK/PD and safety of ravulizumab in paediatric PNH patients from birth to less than 12 years of age **Study 7** *(same study as Study 6 in 001943-PIP01-16-M05 and subsequent modifications thereof)* *(This study was added as a result of procedure 002077-PIP01-16-M03.)* Modelling and simulation study to evaluate the use of subcutaneous ravulizumab in PNH and aHUS in children from 2 years to less than 18 years of age **Study 8** *(same study as Study 7 in 001943-PIP01-16-M05 and subsequent modifications thereof)* *(This study was added as a result of procedure 002077-PIP01-16-M03.)* Extrapolation study to evaluate the use of subcutaneous ravulizumab in children from 2 years to less than 18 years of age with aHUS or paroxysmal nocturnal haemoglobinuria (PNH)

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 2023
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):

Treatment of paroxysmal nocturnal haemoglobinuria (PNH)

Authorised indication(s):

- Treatment of paroxysmal nocturnal haemoglobinuria (PNH) in adult patients with haemolysis with clinical symptom(s) indicative of high disease activity
- Treatment of paroxysmal nocturnal haemoglobinuria (PNH) in adult patients who are clinically stable after having been treated with eculizumab for at least the past 6 months

Treatment of atypical haemolytic uremic syndrome (aHUS)

Authorised indication(s):

- Treatment of patients with a body weight of 10 kg or above with atypical haemolytic uremic syndrome (aHUS) who are complement inhibitor treatment-naïve or have received eculizumab for at least 3 months and have evidence of response to eculizumab

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use