EMA/494329/2023

European Medicines Agency decision

P/0482/2023

of 30 November 2023

on the acceptance of a modification of an agreed paediatric investigation plan for ravulizumab (Ultomiris), (EMEA-001943-PIP04-20-M01) 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/0474/2021 issued on 21 December 2021,

Having regard to the application submitted by Alexion Europe SAS on 3 July 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 13 October 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 ravulizumab (Ultomiris), 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0034/2017 issued on 30 January 2017, decision P/0199/2017 issued on 14 July 2017, and decision P/0230/2021 issued on 08 June 2021, including subsequent modifications thereof.

Article 3

This decision is addressed to Alexion Europe SAS, 103-105 rue Anatole France, 92300 - Levallois-Perret, France.

EMA/PDCO/321359/2023 Corr[1]
Amsterdam, 13 October 2023

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

EMEA-001943-PIP04-20-M01

Scope of the application

Active substance(s):

Ravulizumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of neuromyelitis optica spectrum disorders

Pharmaceutical form(s):

Concentrate for solution for infusion.

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Alexion Europe SAS

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 3 July 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/0474/2021 issued on 21 December 2021.

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

The procedure started on 14 August 2023.

[1] 28 November 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 neuromyelitis optica spectrum disorders

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- 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 neuromyelitis optica spectrum disorders

2.1.1. Indication(s) targeted by the PIP

Treatment of aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder

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

From 2 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	Not applicable.
Clinical studies	**Study 1** (ALXN1210-NMO-317) Open-label, historical-controlled trial to evaluate efficacy, pharmacokinetics, pharmacodynamics, and safety of ravulizumab in children and adolescents from 2 years to less than 18 years of age with aquaporin-4 antibody positive [AQP4-Ab (+)] neuromyelitis optica spectrum disorder (NMOSD)
Extrapolation, modelling and simulation studies	**Study 2** Extrapolation study to evaluate the pharmacokinetics (PK)/ pharmacodynamics (PD), safety and efficacy of ravulizumab in

	paediatric patients with AQP4-Ab (+) NMOSD from 2 years to less than 18 years of age
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 2026
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 paroxysmal nocturnal haemoglobinuria (PNH)

Authorised indication(s):

- Treatment of adult and paediatric patients with a body weight of 10 kg or above with paroxysmal nocturnal haemoglobinuria (PNH): in patients with haemolysis with clinical symptom(s) indicative of high disease activity; in patients who are clinically stable after having been treated with eculizumab for at least the past 6 months
  - Invented name(s): Ultomiris
  - Authorised pharmaceutical form(s): Concentrate for solution for infusion 300 mg/3 mL, 1,100 mg/11 mL and 300 mg/30 mL
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure
- Treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH): in patients with haemolysis with clinical symptom(s) indicative of high disease activity; in patients who are clinically stable after having been treated with eculizumab for at least the past 6 months
  - Invented name(s): Ultomiris
  - Authorised pharmaceutical form(s): 245 mg solution for injection in cartridge, solution for injection (on-body injector)
  - Authorised route(s) of administration: subcutaneous use
  - Authorised via centralised procedure

2. 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
  - Invented name(s): Ultomiris
  - Authorised pharmaceutical form(s): Concentrate for solution for infusion 300 mg/3 mL; 1,100 mg/11 mL and 300 mg/30 mL
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure
- Treatment of adult patients 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
  - Invented name(s): Ultomiris
  - Authorised pharmaceutical form(s): 245 mg solution for injection in cartridge, solution for injection (on-body injector)

- Authorised route(s) of administration: subcutaneous use
- Authorised via centralised procedure

3. Treatment of myasthenia gravis (gMG)

Authorised indication(s):

- Add-on to standard therapy for the treatment of adult patients with gMG who are anti-acetylcholine receptor (AChR) antibody-positive
  - Invented name(s): Ultomiris
  - Authorised pharmaceutical form(s): Concentrate for solution for infusion 300 mg/3 mL; 1,100 mg/11 mL and 300 mg/30 mL
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure

4. Treatment of neuromyelitis optica spectrum disorder (NMOSD)

Authorised indication(s):

- Treatment of adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive
  - Invented name(s): Ultomiris
  - Authorised pharmaceutical form(s): Concentrate for solution for infusion 300 mg/3 mL; 1,100 mg/11 mL and 300 mg/30 mL
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure