EMADOC-1700519818-2034248

European Medicines Agency decision

EMA/PE/0000229605

of 14 April 2025

on the acceptance of a modification of an agreed paediatric investigation plan for ravulizumab (Ultomiris) 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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on the acceptance of a modification of an agreed paediatric investigation plan for ravulizumab (Ultomiris) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0399/2021 issued on 30 September 2021, the decision P/0189/2022 issued on 10 June 2022 and the decision P/0128/2023 issued on 14 April 2023,

Having regard to the application submitted by Alexion Europe on 25 November 2024 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 28 February 2025, 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), 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 30/01/2017, the decision P/0230/2021 issued on 08/06/2021, the decision P/0474/2021 issued on 21/12/2021 and the decision P/0199/2017 issued on 14/07/2017, including subsequent modifications thereof.

Article 3

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

EMADOC-1700519818-1803865
Amsterdam, 28 February 2025

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

EMA/PE/0000229605

Scope of the application

Active substance(s):

Ravulizumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment in haematopoietic stem cell transplantation

Pharmaceutical form(s):

Solution for injection

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Alexion Europe

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Alexion Europe submitted to the European Medicines Agency on 25 November 2024 an application for modification of the agreed paediatric investigation plan with a waiver as set out in the European Medicines Agency's decision P/0399/2021 issued on 30 September 2021, the decision P/0189/2022 issued on 10 June 2022 and the decision P/0128/2023 issued on 14 April 2023.

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

The procedure started on 2 January 2025.

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 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 in haematopoietic stem cell transplantation

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- concentrate for solution for infusion, solution for injection, intravenous use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment in haematopoietic stem cell transplantation

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with haematopoietic stem cell transplant associated thrombotic microangiopathy (HSCT-TMA)

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

From 28 days 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	Description
Quality-related studies	Not applicable.
Non-clinical studies	Not applicable.
Clinical studies	**Study 1 (ALXN1210-TMA-314):** Open-label, single-arm trial to evaluate efficacy, safety, pharmacokinetics and pharmacodynamics of ravulizumab as add-on to best supportive care (BSC) in paediatric patients from 28 days to less than 18 years of age with thrombotic microangiopathy (TMA) after haematopoietic stem cell transplantation (HSCT).

	Study 2 (ALXN1210-TMA-313): Double-blind, randomised, placebo-controlled trial to evaluate efficacy and safety of ravulizumab in adolescents from 12 years to less than 18 years of age (and adults) with thrombotic microangiopathy (TMA) after haematopoietic stem cell transplantation (HSCT).
Modelling and simulation analyses	Not applicable.
Other studies	**Study 3:** Extrapolation study to support extrapolation of efficacy, pharmacokinetics/pharmacodynamics, and safety of ravulizumab in patients with HSCT-TMA from 28 days to less than 18 years of age. (This study was added in February 2025 as a result of procedure EMA-PE-0000229605.)
Extrapolation plan	Studies 1, 2 and 3 are part of the extrapolation plan of pharmacokinetics/pharmacodynamics, safety and efficacy data covering the paediatric population from 28 days to less than 18 years of age with HSCT-TMA. (This extrapolation plan was added in February 2025 as a result of procedure EMA-PE-0000229605.)

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By March 2026
Deferral for one or more measures contained in the paediatric investigation plan:	No

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):

- Ultomiris is indicated in the 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):
        - Ultomiris 300 mg/3 mL concentrate for solution for infusion
        - Ultomiris 1 100 mg/11 mL concentrate for solution for infusion
        - Ultomiris 300 mg/30 mL concentrate for solution for infusion
    - Authorised route(s) of administration: intravenous use after dilution
    - Authorised via centralised procedure

2. Treatment of haemolytic uremic syndrome (aHUS)

Authorised indication(s):

- Ultomiris is indicated in the 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):
        - Ultomiris 300 mg/3 mL concentrate for solution for infusion
        - Ultomiris 1 100 mg/11 mL concentrate for solution for infusion
        - Ultomiris 300 mg/30 mL concentrate for solution for infusion
    - Authorised route(s) of administration: intravenous use after dilution
    - Authorised via centralised

3. Generalised myasthenia gravis (gMG):

Authorised indication(s):

- Ultomiris is indicated as an 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):

- Ultomiris 300 mg/3 mL concentrate for solution for infusion
- Ultomiris 1 100 mg/11 mL concentrate for solution for infusion
- Ultomiris 300 mg/30 mL concentrate for solution for infusion

- Authorised route(s) of administration: intravenous use after dilution
- Authorised via centralised procedure

4. Neuromyelitis optica spectrum disorder (NMOSD):

Authorised indication(s):

Ultomiris is indicated in the treatment of adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive.

- Invented name(s): Ultomiris
- Authorised pharmaceutical form(s):
- Ultomiris 300 mg/3 mL concentrate for solution for infusion
- Ultomiris 1 100 mg/11 mL concentrate for solution for infusion
- Ultomiris 300 mg/30 mL concentrate for solution for infusion
- Authorised route(s) of administration: intravenous use after dilution
- Authorised via centralised procedure