EMA/506319/2024

European Medicines Agency decision

P/0387/2024

of 8 November 2024

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for ravulizumab (Ultomiris), (EMEA-001943-PIP07-24) 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 application submitted by Alexion Europe SAS on 19 January 2024 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 October 2024, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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

A paediatric investigation plan for ravulizumab (Ultomiris), concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for ravulizumab (Ultomiris), concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for ravulizumab (Ultomiris), concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

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, the decision P/0230/2021 issued on 08/06/2021, the decision P/0474/2021 issued on 21 December 2021, including subsequent modifications thereof.

Article 5

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

EMA/PDCO/327872/2024
Amsterdam, 18 October 2024

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001943-PIP07-24

Scope of the application

Active substance(s):

Ravulizumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of primary immunoglobulin A nephropathy

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 16(1) of Regulation (EC) No 1901/2006 as amended, Alexion Europe SAS submitted for agreement to the European Medicines Agency on 19 January 2024 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 26 February 2024.

Supplementary information was provided by the applicant on 4 July 2024. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 primary immunoglobulin A nephropathy

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- 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 primary immunoglobulin A nephropathy

2.1.1. Indication(s) targeted by the PIP

Treatment of primary immunoglobulin A nephropathy (IgAN)

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:** Open-label, uncontrolled, single-arm, multicentre study to evaluate pharmacokinetics, pharmacodynamics, safety, and efficacy of ravulizumab in children and adolescents from 2 years to less than 18 years of age with primary immunoglobulin A nephropathy (IgAN).
Modelling and simulation analyses	**Study 2:** Modelling and simulation study to confirm the paediatric doses for use in children and adolescents from 2 years to less than 18 years of age with IgAN.

Other studies	Not applicable.
Extrapolation plan	Study 1 and Study 2 are part of an extrapolation plan covering the paediatric population from 2 years to less than 18 years of age, as agreed by the PDCO.

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 August 2029
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 adults and paediatric patients with body weight of 10 kg or above with 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
    - Authorised route(s) of administration: Intravenous use
    - Authorised via centralised procedure

2. Treatment of haemolytic uremic syndrome (aHUS)

Authorised indication(s):

- Treatment of patients with a body weight of 10 kg or above with aHUS who are complement inhibitor treatment-naïve or have received eculizumab fo at least 3 months and have evidence of response to eculizumab.
  - Invented name(s): Ultomiris
  - Authorised pharmaceutical form(s): Concentrate for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure

3. Treatment of generalised myasthania gravis (gMG)

Authorised indication(s):

- 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): Concentrate for solution for infusion
  - Authorised route(s) of administration: Intavenous
  - 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
  - Authorised route(s) of administration: Intravenous
  - Authorised via centralised procedure