EMADOC-1700519818-1807955

European Medicines Agency decision

EMA/PE/0000221296

of 3 January 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/0034/2017 issued on 30 January 2017, the decision P/0261/2018 issued on 15 August 2018, the decision P/0199/2019 issued on 12 June 2019, the decision P/0400/2020 issued on 23 October 2020, decision P/0238/2021 issued on 17 June 2021, the decision P/0188/2022 issued on 10 June 2022 and the decision P/0379/2023 issued on 8 September 2023,

Having regard to the application submitted by Alexion Europe on 7 August 2024 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 15 November 2024, 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 and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan including changes to the deferral.

[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), including changes to the deferral, 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/0199/2017 issued on 14 July 2017 and in the decision P/0230/2021 issued on 8 June 2021 and in the decision P/0474/2021 issued on 21 December 2021, including subsequent modifications thereof.

Article 3

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

EMADOC-1700519818-1677812 [1] Corr [2]
Amsterdam, 15 November 2024

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

EMA/PE/0000221296

Scope of the application

Active substance(s):

Ravulizumab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of atypical haemolytic uremic syndrome

Pharmaceutical form(s):

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 7 August 2024 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0034/2017 issued on 30 January 2017, the decision P/0261/2018 issued on 15 August 2018, the decision P/0199/2019 issued on 12 June 2019, the decision P/0400/2020 issued on 23 October 2020, decision P/0238/2021 issued on 17 June 2021, the decision P/0188/2022 issued on 10 June 2022 and the decision P/0379/2023 issued on 8 September 2023.

[1] 26 November 2024
[2] 12 December 2024

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

The procedure started on 16 September 2024.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

One of the pharmaceutical forms and route of administration was deleted.

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 and to the deferral 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 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 atypical haemolytic uremic syndrome (aHUS)

2.1.1. Indication(s) targeted by the PIP

Treatment of atypical haemolytic uremic syndrome

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

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 4** *(Same study as Study 5 in 002077-PIP01-16-M03 and subsequent modifications thereof)* *This study was added as a result of procedure 001943-PIP01-16-M05.* *This study was deleted as a result of procedure EMA/PE/0000221296 - 15 Nov 2024*
Non-clinical studies	Not applicable
Clinical studies	**Study 1** *(ALXN1210-aHUS-312)* *This study was deleted during procedure EMEA-001943-PIP01-16-M01*. **Study 2 (ALXN1210-aHUS-312)** Open-label, single-arm study to evaluate pharmacokinetics, pharmacodynamics, efficacy and safety of ravulizumab following intravenous administration in children from birth to less than 18 years of age with aHUS. **Study 5 (ALXN1210-PED-316)** *(Same study as Study 6 in 002077-PIP01-16-M03 and subsequent modifications thereof)* *This study was added as a result of procedure 001943-PIP01-16-M05.*

	This study was deleted as a result of procedure EMA/PE/0000221296 – 15 Nov 2024.
Extrapolation, modelling and simulation studies	**Study 3** *(Same study as Study 2 in 002077-PIP01-16-M03 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 6** *(Same study as Study 7 in 002077-PIP01-16-M03 and subsequent modifications thereof)* *This study was added as a result of procedure 001943-PIP01-16-M05.* *This study was deleted as a result of procedure EMA/PE/0000221296 – 15 Nov 2024* **Study 7** *(Same study as Study 8 in 002077-PIP01-16-M03 and subsequent modifications thereof)* *This study was added as a result of procedure 001943-PIP01-16-M05.* *This study was deleted as a result of procedure EMA/PE/0000221296 – 15 Nov 2024.*
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 December 2020
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 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 pharmaceutical form(s): Concentrate for solution for infusion
  - Authorised route(s) of administration: Intravenous 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 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 pharmaceutical form(s): Concentrate for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure

3. Treatment of Generalized myasthenia gravis (gMG)

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

4. Treatment of Neuromyelitis optica spectrum disorder (NMOSD)

- Treatment of adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive
  - Invented name(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 pharmaceutical form(s): Concentrate for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure