EMA/627447/2021 Corr

European Medicines Agency decision

P/0474/2021

of 21 December 2021

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-PIP04-20) 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.

European Medicines Agency decision

P/0474/2021

of 21 December 2021

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-PIP04-20) 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 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 application submitted by Alexion Europe SAS on 12 February 2021 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 17 December 2021, 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, 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.
[2] OJ L 136, 30.4.2004, p. 1.

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 decision P/0034/2017 issued on 30 January 2017, and decision P/0199/2017 issued on 14 July 2017, including subsequent modifications thereof.

Article 5

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

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/761092/2021
Amsterdam, 17 December 2021

Final opinion of the Paediatric Committee on the agreement of a Paediatric Investigation plan and a deferral and a waiver

EMEA-001943-PIP04-20

Scope of the application

Active substance(s):

Ravulizumab

Invented name:

Ultomiris

Condition(s):

Treatment of neuromyelitis optica spectrum disorders

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous 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 16(1) of Regulation (EC) No 1901/2006 as amended, Alexion Europe SAS submitted for agreement to the European Medicines Agency on 12 February 2021 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.

An Opinion was adopted by the Paediatric Committee on 15 October 2021 for the above-mentioned product. Alexion Europe SAS received the Paediatric Committee Opinion on 25 October 2021.

On 23 November 2021 Alexion Europe SAS submitted to the European Medicines Agency a written request, including detailed grounds for re-examination of the Opinion.

The re-examination procedure started on 24 November 2021.

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   1.1. to maintain its opinion and

   - 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 Regulation (EC) No 1901/2006 as amended, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member 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 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	**Number of measures**	**Description**
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 1** (ALXN1210-NMO-30X) 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	1	**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	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 June 2026
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):

1. Treatment of paroxysmal nocturnal haemoglobinuria

Authorised indication:

- Ultomiris is indicated in the 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.

2. Treatment of atypical haemolytic uremic syndrome

Authorised indication:

- Ultomiris is indicated in the treatment of patients with a body weight of 10 kg or above with atypical haemolytic uraemic syndrome (aHUS) who are complement inhibitor treatment-naïve or have received eculizumab for at least 3 months and have evidence of response to eculizumab (see section 5.1).

Authorised pharmaceutical form(s):

Concentrate for solution for infusion

Authorised route(s) of administration:

Intravenous use