



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

EMA/251270/2022

## European Medicines Agency decision P/0189/2022

of 10 June 2022

on the acceptance of a modification of an agreed paediatric investigation plan for ravulizumab (Ultomiris), (EMA-001943-PIP02-20-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<sup>1</sup>,

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<sup>2</sup>,

Having regard to the European Medicines Agency's decision P/0399/2021 issued on 30 September 2021,

Having regard to the application submitted by Alexion Europe SAS on 20 January 2022 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 22 April 2022, 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.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1, as amended.

<sup>2</sup> 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), solution for injection, 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/0199/2017 issued on 14 July 2017 and in the decision P/0034/2017 issued on 30 January 2017, including subsequent modifications thereof.

**Article 3**

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/74199/2022  
Amsterdam, 22 April 2022

## Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-001943-PIP02-20-M01

### Scope of the application

#### Active substance(s):

Ravulizumab

#### Invented name:

Ultomiris

#### Condition(s):

Treatment of patients with haematopoietic stem cell transplant associated thrombotic microangiopathy

#### Authorised indication(s):

See Annex II

#### 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 SAS

#### Information about the authorised medicinal product:

See Annex II



## **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 20 January 2022 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 application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 21 February 2022.

## **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 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        | <b>Study 1 (ALXN1210-TMA-314):</b><br><br>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) |

|                                                 |                                                                                                                                                                                                                                                                                                                |
|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                 | <b>Study 2 (ALXN1210-TMA-313):</b><br><br>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) |
| Extrapolation, modelling and simulation studies | Not applicable.                                                                                                                                                                                                                                                                                                |
| 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: | No               |
| Date of completion of the paediatric investigation plan:                              | By November 2024 |
| Deferral for one or more measures contained in the paediatric investigation plan:     | No               |

## **Annex II**

### **Information about the authorised medicinal product**

**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.

## 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.

**Authorised pharmaceutical form(s):**

Concentrate for solution for infusion

**Authorised route(s) of administration:**

Intravenous use