EMA//21389/2023

European Medicines Agency decision

P/0056/2023

of 30 January 2023

on the acceptance of a modification of an agreed paediatric investigation plan for crovalimab (EMEA-002709-PIP01-19-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.

European Medicines Agency decision

P/0056/2023

of 30 January 2023

on the acceptance of a modification of an agreed paediatric investigation plan for crovalimab (EMEA-002709-PIP01-19-M01) 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/0124/2021 issued on 17 March 2021.

Having regard to the application submitted by Roche Registration GmbH on 9 September 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 December 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.

[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 crovalimab, solution for injection/infusion, intravenous use, subcutaneous 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 is addressed to Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/792080/2022 Corr[1]
Amsterdam, 16 December 2022

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

EMEA-002709-PIP01-19-M01

Scope of the application

Active substance(s):

Crovalimab

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of paroxysmal nocturnal haemoglobinuria

Treatment of atypical haemolytic uremic syndrome

Pharmaceutical form(s):

Solution for injection/infusion

Route(s) of administration:

Intravenous use

Subcutaneous use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted to the European Medicines Agency on 9 September 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0124/2021 issued on 17 March 2021.

[1] 25 January 2023

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

The procedure started on 17 October 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 members of Liechtenstein and Norway agree 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 of paroxysmal nocturnal haemoglobinuria

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection/infusion, intravenous use, subcutaneous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

1.2. Condition:

Treatment of atypical haemolytic uremic syndrome

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- solution for injection/infusion, intravenous use, subcutaneous 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 paroxysmal nocturnal haemoglobinuria

2.1.1. Indication(s) targeted by the PIP

Treatment of paroxysmal nocturnal haemoglobinuria (PNH)

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)

Solution for injection/infusion

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable

Non-clinical studies	**Study 1** *(Same study as for condition "treatment of atypical haemolytic uremic syndrome")* Enhanced subcutaneous study to evaluate effects on pre- and post-natal development in Cynomolgus monkeys
Clinical studies	**Study 2 (BO42161)** Open-label, randomised, active controlled trial to evaluate safety and efficacy of crovalimab compared to eculizumab in paediatric patients from 2 years to less than 18 years of age (and adults) with paroxysmal nocturnal haemoglobinuria (PNH) currently treated with complement inhibitors (paediatric patients in descriptive uncontrolled arm only) **Study 3 (BO42162, COMMODORE 2**) Open-label, randomised, active controlled trial to evaluate efficacy and safety of crovalimab compared to eculizumab in paediatric patients from 2 years to less than 18 years of age (and adults) with paroxysmal nocturnal haemoglobinuria (PNH) not previously treated with complement inhibitors (paediatric patients in descriptive uncontrolled arm)
Extrapolation, modelling and simulation studies	**Study 6** *(Same study as for condition "treatment of atypical haemolytic uremic syndrome")* Modelling and simulation study to evaluate the use of crovalimab in children from 2 years to less than 18 years of age with either paroxysmal nocturnal haemoglobinuria (PNH) or atypical haemolytic uremic syndrome (aHUS) **Study 7** *(Same study as for condition "treatment of atypical haemolytic uremic syndrome")* Extrapolation study to evaluate the use of crovalimab in children from 2 years to less than 18 years of age with either paroxysmal nocturnal haemoglobinuria (PNH) or atypical haemolytic uremic syndrome (aHUS)
Other studies	Not applicable
Other measures	Not applicable

2.2. Condition:

Treatment of atypical haemolytic uremic syndrome

2.2.1. Indication(s) targeted by the PIP

Treatment of atypical haemolytic uremic syndrome (aHUS)

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

From 28 days to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Solution for injection/infusion

2.2.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** *(Same study as for condition "treatment of paroxysmal nocturnal haemoglobinuria")* Enhanced subcutaneous study to evaluate effects on pre- and post-natal development in Cynomolgus monkeys
Clinical studies	**Study 4 (BO42353)** Single-arm trial to evaluate pharmacokinetics, efficacy and safety of crovalimab in paediatric patients from 12 years to less than 18 years of age and weighing 40 kg or more (and adults) with atypical haemolytic uremic syndrome (aHUS) **Study 5 (BO42354)** Single-arm trial to evaluate pharmacokinetics, efficacy and safety of crovalimab in paediatric patients from 28 days (and weighing 5 kg or more) to less than 18 years of age with atypical haemolytic uremic syndrome (aHUS)
Extrapolation, modelling and simulation studies	**Study 6** *(Same study as for condition "treatment of paroxysmal nocturnal haemoglobinuria")* Modelling and simulation study to evaluate the use of crovalimab in children from 2 years to less than 18 years of age with either paroxysmal nocturnal haemoglobinuria (PNH) or atypical haemolytic uremic syndrome (aHUS)

	Study 7 *(Same study as for condition "treatment of paroxysmal nocturnal haemoglobinuria")* Extrapolation study to evaluate the use of crovalimab in children from 2 years to less than 18 years of age with either paroxysmal nocturnal haemoglobinuria (PNH) or atypical haemolytic uremic syndrome (aHUS)
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 March 2028
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:

The product is not authorised anywhere in the European Community.