EMA/96085/2021

European Medicines Agency decision

P/0124/2021

of 17 March 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for crovalimab, (EMEA-002709-PIP01-19) 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 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 Roche Registration GmbH on 23 March 2020 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 29 January 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 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 crovalimab, solution for injection/infusion, intravenous use, subcutaneous 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 crovalimab, solution for injection/infusion, intravenous use, subcutaneous 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 crovalimab, solution for injection/infusion, intravenous use, subcutaneous 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 is addressed to Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/597559/2020
Amsterdam, 29 January 2021

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

EMEA-002709-PIP01-19

Scope of the application

Active substance(s):

Crovalimab

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 16(1) of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted for agreement to the European Medicines Agency on 23 March 2020 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 30 April 2020.

Supplementary information was provided by the applicant on 22 October 2020. 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 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 the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex 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	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	1	**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	2	**Study 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) currently treated with complement inhibitors (paediatric patients in descriptive uncontrolled arm only) **Study 3** 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 only)
Extrapolation, modelling and simulation studies	2	**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	0	Not applicable
Other measures	0	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	**Number of measures**	**Description**
Quality-related studies	0	Not applicable
Non-clinical studies	1	**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	2	**Study 4** 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** 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	2	**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	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:	No
Date of completion of the paediatric investigation plan:	By March 2028
Deferral for one or more measures contained in the paediatric investigation plan:	Yes