MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan

MHRA-100816-PIP01-22-M01

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 infusion, Solution for injection

Route(s) of Administration

INTRAVENOUS USE; SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Roche Products Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Roche Products Limited submitted to the licensing authority on 19/12/2022 17:34 GMT an application for a

The procedure started on 13/02/2023 17:34 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100816-PIP01-22-M01

Of 10/03/2023 15:36 GMT

On the adopted decision for crovalimab (MHRA-100816-PIP01-22-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a for crovalimab, Solution for infusion, Solution for injection , INTRAVENOUS, SUBCUTANEOUS USE .

This decision is addressed to Roche Products Limited, 6 Falcon Way, Shire Park, Welwyn Garden City, UNITED KINGDOM, AL7 1TW

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of paroxysmal nocturnal haemoglobinuria (PNH) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Solution for infusion Solution for injection Route(s) of administration: INTRAVENOUS USE SUBCUTANEOUS USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible Condition 2: Treatment of atypical haemolytic uremic syndrome (aHUS) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 28 days of age Pharmaceutical form(s): Solution for infusion Solution for injection Route(s) of administration: INTRAVENOUS USE SUBCUTANEOUS USE Reason for granting waiver: 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(s):

Condition 1: Treatment of paroxysmal nocturnal haemoglobinuria (PNH) Condition 2: Treatment of atypical haemolytic uremic syndrome

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of paroxysmal nocturnal haemoglobinuria (PNH) Condition 2: Treatment of atypical haemolytic uremic syndrome

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

For both Conditions: The paediatric population from 28 days to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both Conditions: Solution for infusion Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	1	Study 1 (Same study for both Conditions) Enhanced subcutaneous study to evaluate effects on pre- and post-natal development in Cynomolgus monkeys.
Clinical Studies	4	Study 2 (Study for Condition 1) 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 (Study for Condition 1) 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). Study 4 (Study for Condition 2) 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 (Study for Condition 2) 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, Modeling & Simulation Studies	2	Study 6 (Same study for both Conditions) 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 for both Conditions) 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 a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	31/03/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes