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-100213-PIP01-21-M03) and to the deferral.

MHRA-100213-PIP01-21-M04

Scope of the Application

Active Substance(s)

RAVULIZUMAB

Condition(s)

Treatment of Paroxysmal Nocturnal Haemoglobinuria

Pharmaceutical Form(s)

Solution for injection. Concentrate for solution for infusion.

Route(s) of Administration

SUBCUTANEOUS USE. INTRAVENOUS USE.

Name / Corporate name of the PIP applicant

Alexion Europe SAS

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Alexion Europe SAS submitted to the licensing authority on 18/01/2024 16:27 GMT an application for a

The procedure started on 05/03/2024 14:32 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 and to the deferral.

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-100213-PIP01-21-M04

Of 27/03/2024 11:48 GMT

On the adopted decision for RAVULIZUMAB (MHRA-100213-PIP01-21-M04) 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 RAVULIZUMAB, Solution for injection. Concentrate for solution for infusion. , SUBCUTANEOUS USE, INTRAVENOUS .

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

ANNEX I

1. Waiver

1.1 Condition:

Not applicable.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of Paroxysmal Nocturnal Haemoglobinuria (PNH).

2.2 Indication(s) targeted by the PIP:

Treatment of Paroxysmal Nocturnal Haemoglobinuria.

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

The paediatric population from birth to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Solution for injection. Concentrate for solution for infusion.

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 5 Development of an age-appropriate subcutaneous formulation. Same as Study 4 in MHRA-100214-PIP01-21-M01 and any subsequent modifications.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 1 (ALXN1210-PNH-304) Open-label multicentre, single arm trial to evaluate pharmacokinetic (PK) and pharmacodynamic (PD) parameters, efficacy and safety of ravulizumab in children from birth to less than 18 years of age with PNH. Study 6 (ALXN1210-PED-316) Open-label multicentre, study to evaluate pharmacokinetics, pharmacodynamics, activity and safety of ravulizumab following subcutaneous administration in children from 2 years to less than 18 years of age with atypical haemolytic uraemic syndrome (aHUS) or PNH. Same as Study 5 in MHRA-100214-PIP01-21-M01 and any subsequent modifications.
Extrapolation, Modeling & Simulation Studies	5	Study 2 Modelling and simulation study to evaluate the use of intravenous ravulizumab in children from birth to less than 18 years of age. Same as Study 3 in MHRA-100214-PIP01-21-M01 and any subsequent modifications. Study 3 Extrapolation study to evaluate the efficacy, PK/PD and safety of ravulizumab in paediatric PNH

		patients from 12 years to less than 18 years of age. Study 4 Extrapolation study to evaluate the efficacy, PK/ PD and safety of ravulizumab in paediatric PNH patients from birth to less than 12 years of age. Study 7 Modelling and simulation study to evaluate the use of subcutaneous ravulizumab in children from 2 years to less than 18 years of age in aHUS and PNH. Same as Study 6 in MHRA-100214-PIP01-21-M01 and any subsequent modifications. Study 8 Extrapolation study to evaluate the use of subcutaneous ravulizumab in children from 2 years to less than 18 years of age with aHUS or PNH. Same as Study 7 in MHRA-100214-PIP01-21-M01 and any subsequent modifications.
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:	31/12/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes