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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-100885-PIP01-23

Scope of the Application

Active Substance(s)

Iptacopan

Condition(s)

Treatment of Paroxysmal Nocturnal Haemoglobinuria (PNH)

Pharmaceutical Form(s)

Capsule, hard; Age appropriate formulation

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Novartis Pharmaceuticals UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Novartis Pharmaceuticals UK Limited submitted to the licensing authority on 06/03/2023 15:45 GMT an application for a Paediatric Investigation Plan

The procedure started on 05/07/2023 16:18 BST

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 agree a paediatric investigation plan and grant a deferral and grant a waiver

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-100885-PIP01-23

Of 29/08/2023 15:43 BST

On the adopted decision for Iptacopan (MHRA-100885-PIP01-23) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for Iptacopan, Capsule, hard; Age appropriate formulation , ORAL USE .

This decision is addressed to Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, UNITED KINGDOM, W12 7FQ

ANNEX I

1. Waiver

1.1 Condition:

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): Capsule, hard Age appropriate formulation Route(s) of administration: ORAL USE Reason for granting waiver: 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(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 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard Age appropriate formulation.

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate oral solid dosage form.
Non-Clinical Studies	1	Study 2 Definitive 52-week toxicity study in juvenile dogs with a 27 week recovery period.
Clinical Studies	1	Study 3 Open-label, single-arm study to assess the safety, tolerability and pharmacokinetics of Iptacopan in paediatric paroxysmal nocturnal haemoglobinuria (PNH) patients 2 years to less than 18 years of age. An efficacy extrapolation in the paediatric patients will be performed under the consideration that the relationship established between the iptacopan exposure and haematological response in adult PNH patients will be the same for paediatric patients.
Extrapolation, Modeling & Simulation Studies	3	Study 4 Population PK model to inform the optimal dose for Study 3 for children from 12 years to less than 18 years of age (Cohort 1). Study 5 Population PK model to inform the optimal dose for Study 3 for children from 2 years to less than 12 years of age (Cohort 2). Study 6 Paediatric population PK model to confirm the efficacy extrapolation strategy and confirm similarity of the exposure response relationship in these two populations.
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:	31/12/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes