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 and to the deferral

MHRA-100302-PIP01-21-M01

Scope of the Application

Active Substance(s)

CRIZANLIZUMAB

Condition(s)

Treatment of sickle cell disease

Pharmaceutical Form(s)

Concentrate for solution for infusion

Route(s) of Administration

Intravenous 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 07/10/2021 17:02 BST an application for a

The procedure started on 29/07/2022 15:39 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 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-100302-PIP01-21-M01

Of 20/09/2022 07:26 BST

On the adopted decision for CRIZANLIZUMAB (MHRA-100302-PIP01-21-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 CRIZANLIZUMAB, Concentrate for solution for infusion , Intravenous 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 sickle cell disease The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age Pharmaceutical form(s): Concentrate for solution for infusion Route(s) of administration: Intravenous use Reason for granting waiver: on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of sickle cell disease

2.2 Indication(s) targeted by the PIP:

Prevention of vaso-occlusive crises in patients with sickle cell disease

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	1	Study 1 Enhanced pre- and postnatal development toxicity study in cynomolgus monkeys
Clinical Studies	1	Study 2 (CSEG101B2201) Open-label, uncontrolled trial to evaluate pharmacokinetics, pharmacodynamics and safety of crizanlizumab with or without hydroxyurea/ hydroxycarbamide in children from 6 months to less than 18 years of age with sickle cell disease with vaso-occlusive crisis.
Extrapolation, Modeling & Simulation Studies	2	Study 3 Modelling and simulation study to support the use of crizanlizumab in the prevention of vaso-occlusive crises in children from 6 months to less than 18 years of age with sickle cell disease. Study 4 Extrapolation study to support the use of crizanlizumab in the prevention of vaso-occlusive crises in children from 6 months to less than 18 years of age with sickle cell disease.
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