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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept of change(s) to the agreed paediatric investigation plan (MHRA-100406-PIP01-21-M01) and to the deferral

MHRA-100406-PIP01-21-M02

Scope of the Application

Active Substance(s)

Marstacimab

Condition(s)

Treatment of congenital haemophilia A, Treatment of congenital haemophilia B

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Pfizer Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Pfizer Limited submitted to the licensing authority on 22/03/2023 16:46 GMT an application for a

The procedure started on 05/07/2023 11:39 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-100406-PIP01-21-M02

Of 07/09/2023 17:34 BST

On the adopted decision for Marstacimab (MHRA-100406-PIP01-21-M02) 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 Marstacimab, Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Pfizer Limited, Ramsgate Road, Sandwich, Kent, UNITED KINGDOM, CT13 9NJ

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of congenital haemophilia A Condition 2: Treatment of congenital haemophilia B The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age. Pharmaceutical form(s): Solution for injection Route(s) of administration: SUBCUTANEOUS USE Reason for granting waiver: on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of congenital haemophilia A Condition 2: Treatment of congenital haemophilia B

2.2 Indication(s) targeted by the PIP:

Condition 1: Prophylaxis of bleeding in haemophilia A (factor VIII deficiency), with and without inhibitors. Condition 2: Prophylaxis of bleeding in haemophilia B (factor IX deficiency), with and without inhibitors.

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

The paediatric population from 1 year to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not Applicable.
Non-Clinical Studies	0	Not Applicable.
Clinical Studies	2	Study 1 (87841005) Non-randomised, open-label, intra-patient controlled, one-way, cross-over, single-arm study to evaluate the safety and efficacy of marstacimab prophylaxis versus previous standard of care on-demand and prophylaxis treatment in severe congenital haemophilia A patients and moderately severe to severe congenital haemophilia B patients with and without inhibitors from 12 to less than 18 years of age (and adults). Study 2 (87841008) Non-randomised, open-label, intra-patient controlled, one-way, cross-over, single-arm study with age staggered enrolment, to evaluate the safety and efficacy of marstacimab prophylaxis versus previous standard of care on-demand and prophylaxis treatment in severe congenital haemophilia A and B patients with and without inhibitors from 1 to less than 18 years of age.
Extrapolation, Modeling & Simulation Studies	3	Study 3 (Modelling study 1) Population PK Modelling and Simulation study to evaluate a suitable dose of marstacimab for

		adolescents from 12 years to less than 18 years of age. Study 4 (Modelling study 2) Population PK Modelling and Simulation study to evaluate a suitable dose of marstacimab for children from 1 year to less than 18 years of age. Study 5 (Modelling study 3) Population PK/ PD exposure-response modelling and simulation study to characterise the PK/PD relationship in paediatric haemophilia patients from 1 year to less than 18 years of age (and adults).
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:	30/11/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes