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-101003-PIP01-23-M01

Scope of the Application

Active Substance(s)

garadacimab

Condition(s)

Prevention of hereditary angioedema

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

CSL Behring GmbH

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, CSL Behring GmbH submitted to the licensing authority on 30/05/2023 13:34 BST an application for a

The procedure started on 07/09/2023 08:21 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-101003-PIP01-23-M01

Of 21/09/2023 09:12 BST

On the adopted decision for garadacimab (MHRA-101003-PIP01-23-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 garadacimab, Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to CSL Behring GmbH, Emil-von-Behring-Str. 76, Marburg, GERMANY, 35041

ANNEX I

1. Waiver

1.1 Condition:

Prevention of hereditary angioedema attacks 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 injection Route(s) of administration: SUBCUTANEOUS USE Reason for granting waiver: On the grounds the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Prevention of hereditary angioedema attacks (HAE)

2.2 Indication(s) targeted by the PIP:

Routine prevention of hereditary angioedema attacks

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):

Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of a 100 mg pre-filled syringe in order to obtain an appropriate 1 mL dose for use in the paediatric population from 2 years to less than 12 years of age.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	3	Study 2 (CSL312_3001) Double-blind, randomised, placebo-controlled, parallel-arm, confirmatory study to evaluate the pharmacokinetics, safety and efficacy of garadacimab when administered as a prophylaxis in adolescents from 12 years to less than 18 years of age (and adults) with hereditary angioedema (HAE). Study 3 (CSL312_3002) Open-label, single-arm, intra-patient controlled study to evaluate the long-term safety and efficacy of garadacimab when administered as a prophylaxis in adolescents from 12 years to less than 18 years of age (and adults) with hereditary angioedema (HAE). Study 4 Open-label, intra-patient controlled study to evaluate pharmacokinetics, pharmacodynamics, safety and efficacy of garadacimab when administered as a prophylaxis in children from 2 years to less than 12 years of age with hereditary angioedema (HAE).

Extrapolation, Modeling & Simulation Studies	2	Study 5 Population pharmacokinetic modelling and analyses to describe the pharmacokinetics of garadacimab in adolescent patients from 12 years to less than 18 years of age and adults with hereditary angioedema. Study 6 Analysis of existing in-house exposure data to supporting the extrapolation of PK from adult and adolescent subjects to paediatric subjects from 2 years to less than 12 years of age with hereditary angioedema and inform dose selection for paediatric subjects from 2 years to less than 12 years of age.
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:	No
Date of completion of the paediatric investigation plan:	30/06/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes