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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral.

MHRA-101071-PIP01-23-M01

Scope of the Application

Active Substance(s)

pegzilarginase

Condition(s)

Treatment of hyperargininaemia

Pharmaceutical Form(s)

Solution for injection/ infusion

Route(s) of Administration

INTRAVENOUS USE; SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Immedica Pharma AB

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Immedica Pharma AB submitted to the licensing authority on 29/06/2023 17:43 BST an application for a Modification

The procedure started on 09/10/2023 13:31 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-101071-PIP01-23-M01

Of 12/10/2023 08:43 BST

On the adopted decision for pegzilarginase (MHRA-101071-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 Modification for pegzilarginase, Solution for injection/ infusion , INTRAVENOUS USE; SUBCUTANEOUS USE .

This decision is addressed to Immedica Pharma AB, 805 Las Cimas Parkway, Austin, UNITED STATES OF AMERICA, 113 63

ANNEX I

1. Waiver

1.1 Condition:

Not applicable.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of hyperargininaemia.

2.2 Indication(s) targeted by the PIP:

Treatment of Arginase 1 Deficiency (Hyperargininaemia).

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/ infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 (BCM001) Definitive juvenile pharmacology study in Arginase I deficient mice to determine if pegzilarginase could normalise circulating arginine levels and prolong the life expectancy in the Arg1-/- mouse model. Study 2 (AEB-002-1020) Definitive juvenile toxicity study in rats to evaluate the potential toxicity and toxicokinetics of pegzilarginase.
Clinical Studies	4	Study 3 (CAEB1102-101A) Open-label, single-arm, single dose-escalation and repeat dosing study in children from 2 to less than 18 years of age (and adults) with Arginase 1 deficiency to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of intravenous (IV) administration of pegzilarginase in patients with Arginase 1 Deficiency and hyperargininaemia. Study 4 (CAEB1102-102A) Long term extension study in children from 2 to less than 18 years of age (and adults) with Arginase 1 deficiency who completed study CAEB1102-101A, to evaluate the long-term safety and tolerability of intravenous (IV) and subcutaneous (SC) pegzilarginase administered for up to 3 years. Study 5 (CAEB1102-300A) Randomized, double-blind, placebo-controlled

		study (followed by an open-label extension phase) in children from 2 to less than 18 years of age (and adults) with Arginase 1 deficiency to evaluate the efficacy and safety of intravenous (IV) pegzilarginase. Study 6 (CAEB1102-301A) Open-label, single-arm, non-controlled, repeat dosing study in children from birth to less than 2 years of age with Arginase 1 deficiency to evaluate the safety, pharmacokinetics and activity of subcutaneous (SC) pegzilarginase.
Extrapolation, Modeling & Simulation Studies	1	Study 7 (CAEB1102-301BA) PopPK/PD modelling and simulation study to predict initial paediatric exposures/doses in infants below 2 years of age with Arginase 1 Deficiency (ARG1-D) for clinical study CAEB1102-301A, following SC administration.
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:	31/12/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes