EMA/494317/2023

European Medicines Agency decision

P/0483/2023

of 30 November 2023

on the acceptance of a modification of an agreed paediatric investigation plan for pegzilarginase (EMEA-001925-PIP02-19-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0252/2020 issued on 15 July 2020,

Having regard to the application submitted by Aeglea BioTherapeutics, Inc. on 29 June 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 October 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for pegzilarginase, solution for infusion, solution for injection, intravenous use, subcutaneous use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Immedica Pharma AB, Solnavägen 3H, 113 63 – Stockholm, Sweden.

EMA/PDCO/321303/2023
Amsterdam, 13 October 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001925-PIP02-19-M01

Scope of the application

Active substance(s):

Pegzilarginase

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of hyperargininaemia

Pharmaceutical form(s):

Solution for infusion

Solution for injection

Route(s) of administration:

Intravenous use

Subcutaneous use

Name/corporate name of the PIP applicant:

Immedica Pharma AB

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Aeglea BioTherapeutics, Inc. submitted to the European Medicines Agency on 29 June 2023 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0252/2020 issued on 15 July 2020.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 14 August 2023.

On 29 August 2023 Aeglea BioTherapeutics, Inc. requested to transfer the paediatric investigation plan to Immedica Pharma AB**.**

Scope of the modification

Some timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

Not applicable.

2. Paediatric investigation plan

2.1. Condition:

Treatment of hyperargininaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of Arginase 1 Deficiency (Hyperargininaemia)

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

Solution for infusion

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable.
Non-clinical studies	Study 1 Definitive juvenile pharmacology study in Arginase I deficient mice to determine if pegzilarginase could normalize circulating arginine levels and prolong the life expectancy in the Arg1-/- mouse model (BCM 001). Study 2 Definitive juvenile toxicity study in rats to evaluate the potential toxicity and toxicokinetics of pegzilarginase (AEB-002-1020).
Clinical studies	Study 3 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 (CAEB1102-101A). Study 4 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 (CAEB1102-102A). Study 5 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 (CAEB1102-300A). Study 6 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 (CAEB1102-301A).
Extrapolation, modelling and simulation studies	Study 7 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 (CAEB1102-301BA).
Other studies	Not applicable.
Other measures	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.