EMA/362119/2020

European Medicines Agency decision

P/0252/2020

of 15 July 2020

on the agreement of a paediatric investigation plan and on the granting of a deferral for pegzilarginase (EMEA-001925-PIP02-19) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Aeglea BioTherapeutics, Inc. on 15 July 2019 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 29 May 2020, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for pegzilarginase, solution for infusion, solution for injection, intravenous use, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for pegzilarginase, solution for infusion, solution for injection, intravenous use, subcutaneous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Aeglea BioTherapeutics, Inc., 805 Las Cimas Parkway, Suite 100, 78736 – Austin, USA.

EMA/PDCO/138471/2020 Corr
Amsterdam, 29 May 2020

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral

EMEA-001925-PIP02-19

Scope of the application

Active substance(s):

Pegzilarginase

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:

Aeglea BioTherapeutics, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Aeglea BioTherapeutics, Inc. submitted for agreement to the European Medicines Agency on 15 July 2019 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 20 August 2019.

Supplementary information was provided by the applicant on 24 February 2020. The applicant proposed modifications to the paediatric investigation plan and withdrew its proposed waiver and proposed a deferral.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

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

2. The measures and timelines of the agreed 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 annex 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	Number of Studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	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	4	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	1	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	0	Not applicable.
Other measures	0	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 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes