EMA/71400/2021

European Medicines Agency decision

P/0074/2021

of 17 March 2021

on the acceptance of a modification of an agreed paediatric investigation plan for eladocagene exuparvovec (EMEA-002435-PIP01-18-M02) 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 European Medicines Agency's decision P/0310/2019 issued on 10 September 2019 and the decision P/0080/2020 issued on 18 March 2020,

Having regard to the application submitted by PTC Therapeutic International Limited on 22 October 2020 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 29 January 2021, in accordance with Article 22 of Regulation (EC) No 1901/2006 and Article 13 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 acceptance of changes to the agreed paediatric investigation plan and to the deferral and on the granting of a waiver.

(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.

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

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for eladocagene exuparvovec, solution for infusion, intracerebral 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

A waiver for eladocagene exuparvovec, solution for infusion, intracerebral use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to PTC Therapeutic International Limited, 5th Floor, 3 Grand Canal Plaza, Grand Canal Street Upper, 4 D04 EE70 – Dublin, Ireland.

EMA/PDCO/589225/2020
Amsterdam, 29 January 2021

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

EMEA-002435-PIP01-18-M02

Scope of the application

Active substance(s):

Eladocagene exuparvovec

Condition(s):

Treatment of aromatic L-amino acid decarboxylase deficiency

Pharmaceutical form(s):

Solution for infusion

Route(s) of administration:

Intracerebral use

Name/corporate name of the PIP applicant:

PTC Therapeutic International Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, PTC Therapeutic International Limited submitted to the European Medicines Agency on 22 October 2020 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0310/2019 issued on 10 September 2019 and the decision P/0080/2020 issued on 18 March 2020.

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

The procedure started on 1 December 2020.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A waiver for a new paediatric subset has been added.

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;
   - to grant a waiver for one or more subsets of the paediatric population concluded in accordance with Article 11(1)(c) of Regulation (EC) No 1901/2006 as amended, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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

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

1.1. Condition

Treatment of aromatic L-amino acid decarboxylase deficiency

The waiver applies to:

- the paediatric population from birth to less than 18 months of age;
- solution for infusion, intracerebral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Treatment of aromatic L-amino acid decarboxylase deficiency

2.1.1. Indication(s) targeted by the PIP

Treatment of aromatic L-amino acid decarboxylase deficiency

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

From 18 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	1	**Study 1** Study to compare gene transfer and biodistribution in the CNS of Cynomolgus monkeys following delivery of eladocagene exuparvovec (AGIL-AADC) at a single dose, through three different routes of administration (intra-putamen, intracerebroventricular or intrathecal/intra-cisternal) and to determine the optimal route of administration **Study 2** *Deleted in procedure EMEA-002435-PIP01-18-M02*.

Clinical studies	3	**Study 3 (AADC-1601)** Retrospective single-arm, observational study to summarise data from a single-arm, compassionate use interventional study (AADC-CU) of male and female children from 2 years to less than 18 years of age with severe aromatic L-amino acid decarboxylase (AADC) deficiency for 60 months, conducted in a single centre in Taiwan). **Study 4 (AADC-010)** Open-label, single arm, externally controlled trial to evaluate safety, efficacy, pharmacodynamics and immunogenicity of AGIL-AADC in children from 18 months to less than 18 years of age with severe AADC deficiency **Study 5 (AADC-011)** Open-label, single arm, externally controlled trial to evaluate efficacy and safety of AGIL-AADC in children from 18 months to less than 6 years of age with severe AADC deficiency ***Study 6*** *deleted in procedure EMEA-002435-PIP01-18-M02*
Extrapolation, modelling and simulation studies	0	Not applicable
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:	Yes
Date of completion of the paediatric investigation plan:	By September 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes