EMA/84338/2023

European Medicines Agency decision

P/0075/2023

of 10 March 2023

on the acceptance of a modification of an agreed paediatric investigation plan for eladocagene exuparvovec (Upstaza), (EMEA-002435-PIP01-18-M03) 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/0310/2019 issued on 10 September 2019, the decision P/0080/2020 issued on 18 March 2020 and the decision P/0074/2021 issued on 17 March 2021,

Having regard to the application submitted by PTC Therapeutic International Limited on 21 November 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 20 January 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.

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

[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 eladocagene exuparvovec (Upstaza), solution for infusion, intraputaminal use, 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 PTC Therapeutic International Limited, 5th Floor, 3 Grand Canal Plaza, Grand Canal Street Upper, 4 D04 EE70 – Dublin, Ireland.

EMA/PDCO/925144/2022 Corr[1]
Amsterdam, 20 January 2023

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

EMEA-002435-PIP01-18-M03

Scope of the application

Active substance(s):

Eladocagene exuparvovec

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of aromatic L-amino acid decarboxylase deficiency

Pharmaceutical form(s):

Solution for infusion

Route(s) of administration:

Intraputaminal 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 21 November 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0310/2019 issued on 10 September 2019, the decision P/0080/2020 issued on 18 March 2020 and the decision P/0074/2021 issued on 17 March 2021.

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

The procedure started on 3 January 2023.

[1] 15 February 2023

Scope of the modification

Some measures or timelines of the Paediatric Investigation Plan have been modified.

The route of administration was amended with a new route of administration.

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 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 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 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

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, intraputaminal 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	Description
Quality-related studies	Not applicable
Non-clinical studies	**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	**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	Not applicable
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:	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

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of aromatic L-amino acid decarboxylase (AADC) deficiency

Authorised indication(s):

- Treatment of clinical, molecular, and genetically confirmed diagnosis of aromatic L-amino acid decarboxylase (AADC) deficiency in patients aged 18 months and older.
  - Invented name(s): Upstaza
  - Authorised pharmaceutical form(s): Solution for infusion
  - Authorised route(s) of administration: Intraputaminal use
  - Authorised via centralised procedure