

EMA/476463/2019

European Medicines Agency decision

P/0310/2019

of 10 September 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for Recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein (EMEA-002435-PIP01-18) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by PTC Therapeutics International Limited on 10 September 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 July 2019, 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 recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein, solution for injection, intracerebral use, intracerebroventricular use, intracisternal use, intrathecal 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 recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein, solution for injection, intracerebral use, intracerebroventricular use, intracisternal use, intrathecal 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 PTC Therapeutics International Limited, 5th Floor, 3 Grand Canal Plaza, Grand Canal Street Upper, 4 D04 EE70 - Dublin, Ireland.

EMA/PDCO/225902/2019 Rev
Amsterdam, 26 July 2019

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

EMA-002435-PIP01-18

Scope of the application

Active substance(s):

Recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein

Condition(s):

Treatment of aromatic L-amino acid decarboxylase deficiency

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intracerebral use

Intracerebroventricular use

Intracisternal use

Intrathecal use

Name/corporate name of the PIP applicant:

PTC Therapeutics International Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, PTC Therapeutics International Limited submitted for agreement to the European Medicines Agency on 10 September 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 16 October 2018.

Supplementary information was provided by the applicant on 25 March 2019. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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 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 birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	2	Study 1 Study to compare gene transfer and biodistribution in the CNS of Cynomolgus monkeys following delivery of recombinant adeno-associated viral vector serotype 2 carrying the gene for the human aromatic L-amino acid decarboxylase protein (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 Study to determine the biodistribution and toxicity of AGIL-AADC in Cynomolgus monkeys during 13 weeks after a single injection in the brain at a single dose via the optimal route of administration determined according to Study 1.
Clinical studies	4	Study 3 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. (AADC-1601). Study 4 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. (AADC-010). Study 5 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. (AADC-011). Study 6 Open-label, single arm, externally controlled trial to evaluate safety, tolerability and efficacy of AGIL-AADC in children from birth to less than 18 months of age with AADC deficiency.
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 June 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes