MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100097-PIP01-21-M01

Scope of the Application

Active Substance(s)

eladocagene exuparvovec

Condition(s)

Treatment of Aromatic L-Amino Acid Decarboxylase (AADC) Deficiency

Pharmaceutical Form(s)

Solution for infusion

Route(s) of Administration

Intracerebral use

Name / Corporate name of the PIP applicant

PTC Therapeutics International Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, PTC Therapeutics International Limited submitted to the licensing authority on 19/04/2021 11:21 BST an application for a Modification

The procedure started on 12/11/2021 07:11 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

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

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100097-PIP01-21-M01

Of 19/11/2021 08:31 GMT

On the adopted decision for eladocagene exuparvovec (MHRA-100097-PIP01-21-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for eladocagene exuparvovec, Solution for infusion , Intracerebral use .

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

ANNEX I

1. Waiver

1.1 Condition:

Treatment of Aromatic L-Amino Acid Decarboxylase (AADC) Deficiency The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 18 months of age; Pharmaceutical form(s): Solution for infusion; Route(s) of administration: Intracerebral use; Reason for granting waiver: 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(s):

Treatment of Aromatic L-Amino Acid Decarboxylase (AADC) Deficiency

2.2 Indication(s) targeted by the PIP:

Treatment of Aromatic L-Amino Acid Decarboxylase (AADC) Deficiency

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 18 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	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 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 MHRA-100097-PIP01-21-M01.
Clinical Studies	3	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; Study 4:_ 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 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; Study 6:_ Deleted in procedure MHRA-100097-PIP01-21-M01
Extrapolation, Modeling & Simulation Studies	0	Not applicable
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/09/2021
Deferral of one or more studies contained in the paediatric investigation plan:	Yes