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 (MHRA-100098-PIP01-21-M01) and to the deferral

MHRA-100098-PIP01-21-M02

Scope of the Application

Active Substance(s)

ATALUREN

Condition(s)

Treatment of dystrophinopathy

Pharmaceutical Form(s)

Granules for oral suspension

Route(s) of Administration

ORAL 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 31/05/2023 18:44 BST an application for a Modification

The procedure started on 16/06/2023 08:09 BST

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-100098-PIP01-21-M02

Of 19/06/2023 15:13 BST

On the adopted decision for ATALUREN (MHRA-100098-PIP01-21-M02) 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 ATALUREN, Granules for oral suspension , ORAL 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 dystrophinopathy The waiver applies / applied to: Paediatric Subset(s): Preterm newborn infants; Term newborn infants (from birth to less than 28 days); Infants (from 28 days to less than 6 months). Pharmaceutical form(s): Granules for oral suspension Route(s) of administration: ORAL 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 dystrophinopathy

2.2 Indication(s) targeted by the PIP:

Treatment of nonsense-mutation dystrophinopathy

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Granules for oral suspension

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age appropriate formulation (granules for oral suspension) for children less than 5 years of age.
Non-Clinical Studies	4	Study 2 28-day dose range finding juvenile toxicology and toxicokinetic study of ataluren in Beagle dogs. Study 3 3-month juvenile toxicology and toxicokinetic study of ataluren in Beagle dogs with a 3-month recovery period. Study 8 7-day tolerability and pharmacokinetic study of ataluren in neonatal Beagle dogs. Study 9 28-Day Investigational Juvenile Toxicology and Toxicokinetic Study of Ataluren in Beagle Dogs with an 8-Week Recovery Period.
Clinical Studies	4	Study 4 (PTC124-GD-007-DMD) Randomised, double-blind, placebo-controlled, multicentre, dose-ranging, efficacy and safety trial in patients 5 years of age and older. Study 5 (PTC124-GD-019-DMD) Open-label, long-term extension study (Europe). Study 6 (PTC124-GD-030-DMD) Open-label trial to evaluate safety and pharmacokinetics of ataluren in children from 2 to less than 5 years with Duchenne Muscular Dystrophy. Study 7 Open-label trial to evaluate safety and pharmacokinetics of ataluren in children from 6 months to less than

		2 years with Duchenne Muscular Dystrophy.
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:	31/05/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes