EMA/899031/2022

European Medicines Agency decision

P/0477/2022

of 2 December 2022

on the refusal of a modification of an agreed paediatric investigation plan for ataluren (Translarna), (EMEA-000115-PIP01-07-M12) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/83/2009 issued on 15 May 2009, the decision P/123/2010 issued on 28 July 2010, the decision P/0069/2012 issued on 4 April 2012, the decision P/0202/2012 issued on 30 August 2012, the decision P/0132/2015 issued on 12 June 2015, the decision P/0002/2016 issued on 14 January 2016, the decision P/0122/2016 issued on 29 April 2016, the decision P/0283/2016 issued on 4 November 2016, the decision P/0393/2017 issued on 19 December 2017, the decision P/0335/2019 issued on 11 September 2019 and the decision P/0195/2021 issued on 10 May 2021,

Having regard to the application submitted by PTC Therapeutics International, Limited on 30 June 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 14 October 2022, 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 refusal of changes to the agreed paediatric investigation plan and to the waiver.

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

[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 ataluren (Translarna), granules for oral suspension, oral use, including changes to the waiver, 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, are hereby refused.

Article 2

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/829144/2022
Amsterdam, 14 October 2022

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

EMEA-000115-PIP01-07-M12

Scope of the application

Active substance(s):

Ataluren

Invented name and authorisation status:

See Annex II

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 opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, PTC Therapeutics International, Limited submitted to the European Medicines Agency on 30 June 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/83/2009 issued on 15 May 2009, the decision P/123/2010 issued on 28 July 2010, the decision P/0069/2012 issued on 4 April 2012, the decision P/0202/2012 issued on 30 August 2012, the decision P/0132/2015 issued on 12 June 2015, the decision P/0002/2016 issued on 14 January 2016, the decision P/0122/2016 issued on 29 April 2016, the decision P/0283/2016 issued on 4 November 2016, the decision P/0393/2017 issued on 19 December 2017, the decision P/0335/2019 issued on 11 September 2019 and the decision P/0195/2021 issued on 10 May 2021.

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

The procedure started on 16 August 2022.

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 refuse the changes proposed by the applicant regarding the paediatric investigation plan and the scope of the waiver.

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

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s)) covered by the waiver remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

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 dystrophinopathy

The waiver applies to:

- preterm and term newborn infants (from birth to less than 28 days of age) and infants (from 28 days to less than 6 months of age);
- granules for oral suspension, oral 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 dystrophinopathy

2.1.1. Indication(s) targeted by the PIP

Treatment of nonsense-mutation dystrophinopathy

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Granules for oral suspension

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	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 8** 7-day tolerability and pharmacokinetic study of ataluren in neonatal Beagle dogs **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 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** Randomized, double-blind, placebo-controlled, multicentre, dose-ranging, efficacy and safety trial in patients 5 years of age and older (PTC124-GD-007-DMD) **Study 5** Open-label, long-term extension study (Europe) (PTC124-GD-019-DMD) **Study 6** Open-label trial to evaluate safety and pharmacokinetics of ataluren in children from 2 to less than 5 years with Duchenne Muscular Dystrophy (PTC124-GD-030-DMD) **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

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 2023
Deferral for one or more studies 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 Duchenne muscular dystrophy

Authorised indication(s):

Treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 2 years and older.

- Invented name(s): Translarna
- Authorised pharmaceutical form(s): Granules for oral suspension
- Authorised route(s) of administration: Oral use
- Authorised via centralised procedure