EMA/630765/2022

European Medicines Agency decision

P/0292/2022

of 11 August 2022

on the acceptance of a modification of an agreed paediatric investigation plan for pretomanid (Dovprela), (EMEA-002115-PIP01-17-M05) 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/0058/2019 issued on 26 February 2019, the decision P/0337/2019 issued on 10 September 2019, the decision P/0340/2020 issued on 9 September 2020 and the decision P/0507/2021 issued on 3 December 2021,

Having regard to the application submitted by Global Alliance for TB Drug Development on 21 March 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 June 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 acceptance of changes to the agreed paediatric investigation plan and to the deferral.

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

[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 pretomanid (Dovprela), tablet, dispersible tablet, oral use, including changes to the deferral, 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 Global Alliance for TB Drug Development, 40 Wall Street, NY 10005 - New York, United States.

EMA/PDCO/193887/2022
Amsterdam, 24 June 2022

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

EMEA-002115-PIP01-17-M05

Scope of the application

Active substance(s):

Pretomanid

Invented name

Dovprela

Condition(s):

Treatment of multi-drug-resistant tuberculosis

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Dispersible tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Global Alliance for TB Drug Development

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Global Alliance for TB Drug Development submitted to the European Medicines Agency on 21 March 2022 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0058/2019 issued on 26 February 2019, the decision P/0337/2019 issued on 10 September 2019, the decision P/0340/2020 issued on 9 September 2020 and the decision P/0507/2021 issued on 3 December 2021.

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

The procedure started on 25 April 2022.

Scope of the modification

Some timelines of the Paediatric Investigation Plan have been modified.

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 and to the deferral 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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of multi-drug-resistant tuberculosis

2.1.1. Indication(s) targeted by the PIP

Pretomanid is indicated for use as part of an appropriate combination regimen for pulmonary multi-drug resistant tuberculosis (MDR-TB) when an effective treatment regimen cannot otherwise be composed for reasons of resistance or tolerability.

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)

Tablet

Dispersible tablet

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of dispersible tablet formulation.
Non-clinical studies	**Study 2** Juvenile toxicity study in rats.
Clinical studies	**Study 3 (BA-Study)** An open-label, randomized, 4-period crossover study in 2 panels of healthy, adult subjects to assess the relative bioavailability, food effect, and dose dependence of the formulations of pretomanid. **Study 4 (PAEDIATRIC-1)** An open-label, single-dose study to assess the pharmacokinetics, safety and tolerability of pretomanid in paediatric patients with rifampin-resistant (RR) tuberculosis (TB). **Study 5 (PAEDIATRIC-2)** An open-label, multicenter study to evaluate the pharmacokinetics, safety, tolerability and anti-mycobacterial activity of pretomanid in combination with bedaquiline and linezolid (B-Pa-L) for the treatment of

	paediatric patients with confirmed or probable pulmonary pre-extensively-resistant or extensively drug-resistant tuberculosis (pre-XDR/XDR-TB), or those who have failed or are intolerant to treatment for multidrug-resistant tuberculosis (MDR-TB).
Extrapolation, modelling and simulation studies	**Study 6** Population pharmacokinetic (PK) modelling and simulation study in paediatric patients with pulmonary (with or without extrapulmonary) infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB). **Study 7** Extrapolation study of the clinical efficacy and safety data for pretomanid in combination with bedaquiline and linezolid (B-Pa-L regimen) from adult patients to paediatrics patients with pulmonary (with or without extrapulmonary) infection of either extensively drug-resistant tuberculosis (XDR-TB), pre-XDR-TB or treatment intolerant or non-responsive multi-drug resistant tuberculosis (MDR-TB).
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 February 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of tuberculosis

Authorised indication(s):

- Dovprela is indicated in combination with bedaquiline and linezolid, in adults, for the treatment of pulmonary extensively drug resistant (XDR), or treatment-intolerant or nonresponsive multidrugresistant (MDR) tuberculosis (TB),

Authorised pharmaceutical form(s):

Tablets

Authorised route(s) of administration:

Oral use