EMA/876006/2022

European Medicines Agency decision

P/0505/2022

of 2 December 2022

on the acceptance of a modification of an agreed paediatric investigation plan for doravirine (Pifeltro), (EMEA-001676-PIP01-14-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/0139/2016 issued on 20 May 2016, decision P/0115/2017 issued on 21 April 2017, decision P/0254/2020 issued on 15 July 2020, and decision P/0177/2021 issued on 12 April 2021,

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc. on 4 August 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 11 November 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 doravirine (Pifeltro), tablet, granules, 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 Merck Sharp & Dohme (Europe), Inc., Clos du Lynx, 5, B-1200 – Brussels, Belgium.

EMA/PDCO/695719/2022
Amsterdam, 11 November 2022

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

EMEA-001676-PIP01-14-M05

Scope of the application

Active substance(s):

Doravirine

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of human immunodeficiency virus-1 (HIV-1) infection

Pharmaceutical form(s):

Tablet

Granules

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Merck Sharp & Dohme (Europe), Inc.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe), Inc. submitted to the European Medicines Agency on 4 August 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/0139/2016 issued on 20 May 2016, the decision P/0115/2017 issued on 21 April 2017, decision P/0254/2020 issued on 15 July 2020, and the decision P/0177/2021 issued on 12 April 2021.

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

The procedure started on 12 September 2022.

Scope of the modification

Some measures and 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.
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 human immunodeficiency virus type 1 (HIV-1) infection

2.1.1. Indication(s) targeted by the PIP

Antiretroviral therapy, in combination with other antiretroviral agents, for the treatment of HIV-1 infection in children from birth to 18 years of age

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

Granules

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of an age-appropriate oral solid dosage form.
Non-clinical studies	**Study 2** Dose range-finding juvenile toxicity study. **Study 3** Definitive juvenile toxicity study.
Clinical studies	**Study 4** Open-label two period trial to evaluate pharmacokinetic, safety, and activity, of doravirine and doravirine fixed dose combination with lamivudine and tenofovir disoproxil fumarate in adolescents from 12 to less than 18 years of age weighing at least 35 kg with HIV-1 infection.

	Study 5 Open-label pharmacokinetic with sentinel cohort, safety, and activity study of doravirine in HIV-1 paediatric patients who are at least 4 weeks and less than 12 years of age. ***Study 6*** *Study deleted in EMEA-001676-PIP01-14-M03.* **Study 7** Open-label, 2 period study to assess the pharmacokinetics and safety of doravirine in term neonates born to HIV infected mothers who are at risk of HIV-1 infection vertically transmitted. ***Study 8*** *Study deleted in EMEA-001676-PIP01-14-M04.* ***Study 9*** *Study deleted in EMEA-001676-PIP01-14-M04.*
Extrapolation, modelling and simulation studies	**Study 10** Modelling and simulation and extrapolation study of the use of doravirine in paediatric patients from birth to less than 18 years of age and of the use of the FDC of DOR/3TC/TDF in children from 6 to less than 18 years of age.
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:	No
Date of completion of the paediatric investigation plan:	By November 2028
Deferral for one or more measures 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 HIV-1

Authorised indication(s):

- Pifeltro is indicated, in combination with other antiretroviral medicinal products, for the treatment of adults infected with HIV-1 without past or present evidence of resistance to the NNRTI class

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral route