EMA/251175/2017

European Medicines Agency decision

P/0116/2017

of 28 April 2017

on the acceptance of a modification of an agreed paediatric investigation plan for doravirine / lamivudine / tenofovir disoproxil (fumarate) (EMEA-001695-PIP01-14-M01) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0140/2016 issued on 20 May 2016,

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc on 3 January 2017 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 24 March 2017, 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.

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

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for doravirine / lamivudine / tenofovir disoproxil (fumarate), tablet, granules, oral use, 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/18964/2017
London, 24 March 2017

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

EMEA-001695-PIP01-14-M01

Scope of the application

Active substance(s):

Doravirine / lamivudine / tenofovir disoproxil (fumarate)

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 3 January 2017 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/0140/2016 issued on 20 May 2016.

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

The procedure started on 24 January 2017.

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 in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver 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 annex 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 human immunodeficiency virus-1 (HIV-1) infection

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- granules, for oral use;

  on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

And

- the paediatric population from birth to less than 12 years of age and weighing less than 35Kg;
- tablet, for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

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 combination therapy, for the treatment of HIV-1 infection in adults and in children aged 2 to 18 years

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet

Granules

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral solid dosage form for the fixed dose combination doravirine, lamivudine, tenofovir disoproxil (fumarate).

Non-clinical studies	2	**Study 2** Dose range-finding juvenile toxicity study. **Study 3** Definitive juvenile toxicity study.
Clinical studies	6	**Study 4** Open-label two periods trial to evaluate pharmacokinetic, safety, and activity, of doravirine and doravirine fixed dose combination (FDC) with lamivudine and tenofovir disoproxil (fumarate) in HIV-1 infected adolescents from 12 to less than 18 years of age weighing at least 35 kg. **Study 5** Open-label 2 period pharmacokinetic, safety, and activity study of doravirine and doravirine fixed dose combination with lamivudine and tenofovir disoproxil (fumarate) in HIV-1 children and adolescents who are at least from to 2 years of age and less than the minimum weight threshold for administration of the adult dose as identified in study 4 with HIV-1 infection**.** **Study 6** Relative bioavailability study with doravirine adult oral granules to be part of the fixed dose combination in healthy adults. **Study 7** Relative bioavailability study with doravirine age appropriate oral granules new formulation as be part of the fixed dose combination. **Study 8** Relative bioavailability study with lamivudine and tenofovir disoproxil (fumarate) age appropriate formulations to be part of the fixed dose combination in healthy adults **Study 9** Study deleted in procedure EMEA-001695-PIP01-14-M01.
Extrapolation, modelling and simulation studies	1	**Study 10** Dose finding modelling and simulation study in children from 2 to less than less than 18 years of age.
Other studies	0	Not applicable.
Other measures	0	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 July 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes