



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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European Medicines Agency decision

P/0339/2016

of 2 December 2016

on the acceptance of a modification of an agreed paediatric investigation plan for bictegravir / emtricitabine / tenofovir alafenamide (EMA-001766-PIP01-15-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.



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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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/0316/2015 issued on 21 December 2015,

Having regard to the application submitted by Gilead Sciences International Ltd on 22 July 2016 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 2016, 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 bicittegravir / emtricitabine / tenofovir alafenamide, age-appropriate oral formulation, film coated tablet, 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 Gilead Sciences International Ltd., Granta Park, CB21 6GT – Cambridge, United Kingdom.

EMA/PDCO/534444/2016

London, 14 October 2016

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

EMA-001766-PIP01-15-M01

Scope of the application

Active substance(s):

Bictegravir / emtricitabine / tenofovir alafenamide

Condition(s):

Treatment of human immunodeficiency virus (HIV-1) infection

Pharmaceutical form(s):

Age-appropriate oral formulation

Film-coated tablet

Route(s) of administration:

Oral use

Name / corporate name of the PIP applicant:

Gilead Sciences International Ltd

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Gilead Sciences International Ltd submitted to the European Medicines Agency on 22 July 2016 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/0316/2015 issued on 21 December 2015.

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

The procedure started on 16 August 2016.

Scope of the modification

Some measures 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 (HIV-1) infection

The waiver applies to:

- the paediatric population from birth to less than 4 weeks of age;
- age-appropriate oral formulation, oral use;
- film-coated tablet, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of human immunodeficiency virus (HIV-1) infection

2.1.1. Indication(s) targeted by the PIP

Treatment of human immunodeficiency virus (HIV-1) infection

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

From 4 weeks to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Age-appropriate oral formulation

Film-coated tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	Study 1 Development of film-coated tablets for use in children from 6 to less than 12 years of age Study 2 Development of an age-appropriate oral formulation for use in children from 4 weeks to less than 6 years of age, and in children above 6 years of age unable to swallow tablets.

Non-clinical studies	1	Study 3 Prenatal and postnatal reproductive toxicity study of bictegavir (BIC; GS-9883) in rats [Study 4 deleted in EMEA-001766-PIP01-15-M01]
Clinical studies	3	Study 5 Open-label, single arm trial to evaluate pharmacokinetics, safety, tolerability and efficacy of the bictegavir/ emtricitabine/tenofovir alafenamide (B/F/TAF) fixed-dose combination (FDC) in children from 6 to less than 18 years of age with HIV-1 infection, who are virologically suppressed on an antiretroviral (ARV) regimen. Study 6 Open-label, single arm trial to evaluate pharmacokinetics, safety, tolerability and efficacy of the B/F/TAF FDC in children from 4 weeks to less than 6 years of age with HIV-1 infection, who are treatment-experienced and virologically suppressed, or treatment-naïve (only children less than 6 months of age). Study 7 Open-label, randomised study in healthy adult volunteers to determine the bioavailability of the age-appropriate oral formulation developed in Study 2 relative to the adult film-coated tablet.
Extrapolation, modelling and simulation studies	2	Study 8 Modelling and Simulation study to support dose finding and the extrapolation of use of the B/F/TAF FDC in children from 4 weeks to less than 18 years of age who are infected with HIV-1. Study 9 Extrapolation study to support the use of the B/F/TAF FDC in children from 4 weeks to less than 18 years who are infected with HIV-1 with INSTI resistance.
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:	Yes
Date of completion of the paediatric investigation plan:	By December 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes