EMA/250921/2023

European Medicines Agency decision

P/0242/2023

of 14 June 2023

on the acceptance of a modification of an agreed paediatric investigation plan for bictegravir / emtricitabine / tenofovir alafenamide (Biktarvy), (EMEA-001766-PIP01-15-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/0316/2015 issued on 21 December 2015, the decision P/0339/2016 issued on 2 December 2016, the decision P/0334/2020 issued on 24 August 2020, the decision P/0038/2021 issued on 27 January 2021 and the decision P/0528/2021 issued on 3 December 2021,

Having regard to the application submitted by Gilead Sciences International Ltd on 20 February 2023 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 26 May 2023, 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 bictegravir / emtricitabine / tenofovir alafenamide (Biktarvy), age-appropriate oral formulation, film-coated 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 Gilead Sciences International Ltd., Flowers Building, Granta Park, Great Abington CB21 6GT – Cambridge, United Kingdom.

EMA/PDCO/102969/2023
Amsterdam, 26 May 2023

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

EMEA-001766-PIP01-15-M05

Scope of the application

Active substance(s):

Bictegravir / emtricitabine / tenofovir alafenamide

Invented name and authorisation status:

See Annex II

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 20 February 2023 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 decision P/0339/2016 issued on 2 December 2016, the decision P/0334/2020 issued on 24 August 2020, the decision P/0038/2021 issued on 28 January 2021 and the decision P/0528/2021 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 27 March 2023.

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 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 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 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, 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 in paediatric patients without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

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	Description
Quality-related studies	**Study 1** Development of film-coated tablets of lower strength appropriate for use in children at least 2 years of age and weighing from 14 to less than 25 kg. **Study 2** Development of an age-appropriate oral formulation for use in children at least 4 weeks of age and weighing from 3 to less than 14 kg, and in children weighing less than 25 kg unable to swallow tablets.

Non-clinical studies	**Study 3 (TX-141-2045)** Prenatal and postnatal reproductive toxicity study of bictegravir (BIC; GS-9883) in rats **Study 4** deleted in procedure EMEA-001766-PIP01-15-M01
Clinical studies	**Study 5 (GS-US-380-1474)** Single arm, two-part study to evaluate the pharmacokinetics (part A), safety, tolerability and efficacy (part B) of the bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) fixed-dose combination (FDC) in HIV-1 infected, virologically suppressed adolescents and children down to 2 years of age and weighing at least 14 kg and in infants down to 4 weeks of age and weighing at least 3 kg who have been on an antiretroviral (ARV) regimen at least 1 months prior to screening or are treatment naïve. **Study 6** Study deleted in procedure EMEA-001766-PIP01-15-M02. **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 (GS-US-380-4547).
Extrapolation, modelling and simulation studies	**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** Study deleted in procedure EMEA-001766-PIP01-15-M02.
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 September 2025
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 human immunodeficiency virus (HIV-1) infection

Authorised indication(s):

- Biktarvy is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults and paediatric patients at least 2 years of age and weighing at least 14 kg without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir
  - Invented name(s): Biktarvy
  - Authorised pharmaceutical form(s): film-coated tablet
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure