EMA/519894/2014

European Medicines Agency decision

P/0249/2014

of 30 September 2014

on the acceptance of a modification of an agreed paediatric investigation plan for tenofovir (disoproxil fumarate) (Viread), (EMEA-000533-PIP01-08-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.

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

European Medicines Agency decision

P/0249/2014

of 30 September 2014

on the acceptance of a modification of an agreed paediatric investigation plan for tenofovir (disoproxil fumarate) (Viread), (EMEA-000533-PIP01-08-M05) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/18/2010 issued on 8 February 2010, the decision P/51/2011 issued on 4 March 2011, the decision P/180/2011 issued on 28 July 2011, the decision P/0109/2012 issued on 8 June 2012, and the decision P/0018/2013 issued on 31 January 2013,

Having regard to the application submitted by Gilead Sciences International Limited on 15 May 2014 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 15 August 2014, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for tenofovir (disoproxil fumarate) (Viread), film-coated tablet, oral powder, 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 Limited, Granta Park, Abington, CB21 6GT – Cambridge, United Kingdom.

Done at London, 30 September 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/356592/2014

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

EMEA-000533-PIP01-08-M05

Scope of the application

Active substance(s):

Tenofovir (disoproxil fumarate)

Invented name:

Viread

Condition(s):

Treatment of human immunodeficiency virus (HIV) disease resulting in other conditions

Treatment of chronic viral hepatitis B

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Oral powder

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Gilead Sciences International Limited

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Gilead Sciences International Limited submitted to the European Medicines Agency on 15 May 2014 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/18/2010 issued on 8 February 2010, the decision P/51/2011 issued on 4 March 2011, the decision P/180/2011 issued on 28 July 2011, the decision P/0109/2012 issued on 8 June 2012, and the decision P/0018/2013 issued on 31 January 2013.

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

The procedure started on 18 June 2014.

Scope of the modification

Some timelines of the original 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 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 annexes and appendix.

London, 15 August 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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) disease resulting in other conditions

The waiver applies to:

- children from birth to less than 12 years of age;
- for tenofovir DF film-coated tablet for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1.2. Condition:

Treatment of chronic viral hepatitis B

The waiver applies to:

- children from birth to less than 12 years;
- for tenofovir DF film-coated tablet for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

The waiver applies to:

- infants and toddlers from birth to less than 2 years;
- for tenofovir DF oral powder;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

2. Paediatric investigation plan

2.1. Condition:

Treatment of human immunodeficiency virus (HIV) disease resulting in other conditions

2.1.1. Indication(s) targeted by the PIP

In combination with other antiretroviral medicinal products for the treatment of HIV-1 infection in antiretroviral treatment experienced paediatric patients.

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

1. The paediatric population from 12 years to less than 18 years of age for the film-coated tablets for oral use.
2. All subsets of the paediatric population from birth to less than 18 years of age for the oral powder.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Oral powder

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	3	**Study 1: GS-US-104-0321** Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of Tenofovir DF as Part of an Optimized Antiretroviral Regimen in HIV-1-Infected Adolescents. **Study 2: GS-US- 104-0352** Randomized, Open-Label Study Comparing the Safety and Efficacy of Switching Stavudine or Zidovudine to Tenofovir Disoproxil Fumarate versus Continuing Stavudine or Zidovudine in Virologically Suppressed HIV-Infected Children Taking Highly Active Antiretroviral Therapy. **Study 3:** A safety and pharmacokinetic study of tenofovir DF oral powder in HIV-1 infected subjects < 2 years of age.
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of chronic viral hepatitis B

2.2.1. Indication(s) targeted by the PIP

For treatment of chronic hepatitis B in paediatric patients from 2 years of age with compensated liver disease.

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

1. The paediatric population from 12 years to less than 18 years of age for the film-coated tablets for oral use.
2. All subsets of the paediatric population from 2 years to less than 18 years of age for the oral powder.

2.2.3. Pharmaceutical form(s)

Film-coated tablet

Oral powder

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies		Not applicable.
Non-clinical studies		Not applicable.
Clinical studies	2	**Study 4: GS-US-174-0115.** A Randomized, Double-Blind Evaluation of the Antiviral Efficacy, Safety, and Tolerability of Tenofovir Disoproxil Fumarate Versus Placebo in Adolescents with Chronic Hepatitis B Infection. **Study 5:** A safety and efficacy or pharmacokinetic study of tenofovir DF in children aged 2 to < 12 years with chronic HBV infection. **Study 6:** Randomised open label multicentre study to evaluate efficacy and safety, of tenofovir in children and adolescents with decompensated chronic hepatitis B virus infection in patients aged from 2 to less than 18 years.
Extrapolation, modelling and simulation studies	0	Not applicable.
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 February 2019
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 human immunodeficiency virus (HIV) disease

Authorised indication(s):

- Viread is indicated in combination with other antiretroviral medicinal products for the treatment of HIV 1 infected adults over 18 years of age

2. Treatment of chronic viral hepatitis B

Authorised indication(s):

- Viread is indicated for the treatment of chronic Hepatitis B in adults with compensated liver disease, with evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis.
- Viread is indicated for the treatment of chronic Hepatitis B in adults with decompensated liver disease.

Authorised pharmaceutical form(s):

Film-coated tablet, granules

Authorised route(s) of administration:

Oral use