



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/791470/2015

European Medicines Agency decision

P/0316/2015

of 21 December 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for emtricitabine / tenofovir alafenamide / Sodium (2R,5S, 13aR)-7,9-dioxo-10-[(2,4,6-trifluorobenzyl carbamoyl)-2,3,4,5,7,9,13,13a-octahydro-2,5-methanopyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazepin-8-olate (GS-9883) (EMA-001766-PIP01-15) 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 application submitted by Gilead Sciences International Ltd on 10 April 2015 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 November 2015, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.
- (2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.
- (3) It is therefore appropriate to adopt a decision granting a deferral.
- (4) It is therefore appropriate to adopt a decision granting a waiver.

¹ OJ L 378, 27.12.2006, p.1.

² OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for emtricitabine / tenofovir alafenamide / Sodium (2R,5S, 13aR)-7,9-dioxo-10-[(2,4,6-trifluorobenzyl carbamoyl)-2,3,4,5,7,9,13,13a-octahydro-2,5-methanopyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazepin-8-olate (GS-9883), age-appropriate oral formulation, film-coated tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for emtricitabine / tenofovir alafenamide / Sodium (2R,5S, 13aR)-7,9-dioxo-10-[(2,4,6-trifluorobenzyl carbamoyl)-2,3,4,5,7,9,13,13a-octahydro-2,5-methanopyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazepin-8-olate (GS-9883), age-appropriate oral formulation, film-coated tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for emtricitabine / tenofovir alafenamide / Sodium (2R,5S, 13aR)-7,9-dioxo-10-[(2,4,6-trifluorobenzyl carbamoyl)-2,3,4,5,7,9,13,13a-octahydro-2,5-methanopyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazepin-8-olate (GS-9883), age-appropriate oral formulation, film-coated tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Gilead Sciences International Ltd, Granta Park, CB21 6GT – Cambridge, United Kingdom.

Done at London, 21 December 2015

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/581501/2015
London, 13 November 2015

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMA-001766-PIP01-15

Scope of the application

Active substance(s):

Emtricitabine / tenofovir alafenamide / Sodium (2R,5S, 13aR)-7,9-dioxo-10-[(2,4,6-trifluorobenzyl carbamoyl]-2,3,4,5,7,9,13,13a-octahydro-2,5-methanopyrido[1',2':4,5]pyrazino[2,1-b][1,3]oxazepin-8-olate (GS-9883)

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 16(1) of Regulation (EC) No 1901/2006 as amended, Gilead Sciences International Ltd submitted for agreement to the European Medicines Agency on 10 April 2015 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 19 May 2015.

Supplementary information was provided by the applicant on 21 August 2015. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report :

- to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
- to grant a deferral in accordance with Article 21 of said Regulation;
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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

2. The measures and timelines of the agreed 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	2	Study 3

		Prenatal and postnatal reproductive toxicity study of GS-9883 in rats Study 4 Juvenile toxicity and toxicokinetic study of GS-9883 in rats.
Clinical studies	3	Study 5 Open-label, single arm trial to evaluate pharmacokinetics, safety, tolerability and efficacy of the emtricitabine/tenofovir alafenamide/GS-9883 (F/TAF/GS-9883) 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 F/TAF/GS-9883 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 F/TAF/GS-9883 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 F/TAF/GS-9883 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