EMA/215118/2015

European Medicines Agency decision

P/0099/2015

of 8 May 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for sofosbuvir/a derivative of (S)-methyl (2-(2-(1H-imidazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (GS-5816) (EMEA-001646-PIP01-14) 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 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 application submitted by Gilead Sciences International Ltd. on 9 May 2014 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 20 March 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 sofosbuvir/ a derivative of (S)-methyl (2-(2-(1H-imidazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (GS-5816), film-coated tablet, age-appropriate oral formulation, 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 sofosbuvir/a derivative of (S)-methyl (2-(2-(1H-imidazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (GS-5816), film-coated tablet, age-appropriate oral formulation, 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 sofosbuvir/a derivative of (S)-methyl (2-(2-(1H-imidazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (GS-5816), film-coated tablet, age-appropriate oral formulation, 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., Flowers Building, Granta Park, Abington, CB21 6GT - Cambridge, United Kingdom.

Done at London, 8 May 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/20509/2015
London, 20 March 2015

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

EMEA-001646-PIP01-14

Scope of the application

Active substance(s):

Sofosbuvir/a derivative of (S)-methyl (2-(2-(1H-imidazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (GS-5816)

Condition(s):

Treatment of chronic hepatitis C

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral formulation

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 9 May 2014 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 18 June 2014.

Supplementary information was provided by the applicant on 17 December 2014. The applicant proposed modifications to the paediatric investigation plan.

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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 Icelandic and the Norwegian Paediatric Committee members agree 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 chronic hepatitis C

The waiver applies to:

- the paediatric population from birth to less than 3 years of age;
- film-coated tablet, age-appropriate oral formulation, 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 chronic hepatitis C

2.1.1. Indication(s) targeted by the PIP

Treatment of children and adolescents from 3 years to less than 18 years of age with genotype 1-6 chronic hepatitis C who are treatment-naïve or treatment-experienced

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

From 3 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of a film-coated tablet for use in children from 6 to less than 12 years of age and in adolescents from 12 to less than 18 years of age who are unable to swallow the adult-size tablets. **Study 2** Development of an age-appropriate oral formulation for use in children from 3 to less than 6 years of age, and in children above 6 years of age unable to swallow tablets.
Non-clinical studies	0	Not applicable.

Clinical studies	2	**Study 3** Open-label, randomised trial in healthy adult volunteers to determine the bioavailability of the age-appropriate oral formulation of the sofosbuvir (SOF)/GS-5816 fixed-dose combination (FDC) relative to the adult film-coated tablet **Study 4** Open-label, single arm trial to evaluate pharmacokinetics, safety, antiviral activity and acceptability/palatability of SOF/GS-5816 in children from 3 to less than 18 years of age with chronic hepatitis C genotype 1-6 infection.
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 April 2020
Deferral for one or more measures contained in the paediatric investigation plan:	Yes