



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/265338/2016

European Medicines Agency decision

P/0121/2016

of 29 April 2016

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for sofosbuvir / velpatasvir / a derivative of (2S,3S,4R)-3-ethyl-4-hydroxypyrrolidine-2-carboxylic acid, (EMEA-001822-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 2 July 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 1 April 2016, 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 / velpatasvir / a derivative of (2S,3S,4R)-3-ethyl-4-hydroxypyrrolidine-2-carboxylic acid, film-coated tablet, age-appropriate oral dosage form, 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 / velpatasvir / a derivative of (2S,3S,4R)-3-ethyl-4-hydroxypyrrolidine-2-carboxylic acid, film-coated tablet, age-appropriate oral dosage form, 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 / velpatasvir / a derivative of (2S,3S,4R)-3-ethyl-4-hydroxypyrrolidine-2-carboxylic acid, film-coated tablet, age-appropriate oral dosage form, 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, Abingdon, CB21 6GT – Cambridge, United Kingdom.

Done at London, 29 April 2016

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



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO/6216/2016

London, 1 April 2016

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

EMA-001822-PIP01-15

Scope of the application

Active substance(s):

sofosbuvir / velpatasvir / a derivative of (2S,3S,4R)-3-ethyl-4- hydroxypyrrolidine-2-carboxylic acid

Condition(s):

Treatment of chronic hepatitis C

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral dosage form

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 2 July 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 11 August 2015.

Supplementary information was provided by the applicant on 22 December 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 chronic hepatitis C

The waiver applies to:

- the paediatric population from birth to less than 3 years of age;
- for film-coated tablet and for age-appropriate oral dosage form for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Treatment of chronic hepatitis C

2.1.1. Indication(s) targeted by the PIP

Treatment of chronic hepatitis C

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 dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	Study 1: Development of an age-appropriate oral solid dosage form for children 6 to less than 12 years of age and for adolescents 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 dosage form for children 3 years to less than 6 years of age

Area	Number of measures	Description
Non-clinical studies	0	Not applicable
Clinical studies	2	Study 3: Randomised, open-label, crossover, single-dose comparative bioavailability study of adult versus age-appropriate paediatric formulations of sofosbuvir / velpatasvir / GS-9857 fixed-dose combination (GS-US-367-1174) Study 4: Open-label, 3-cohort study to characterise the pharmacokinetics, safety, antiviral activity and efficacy of sofosbuvir / velpatasvir / GS-9857 fixed-dose combination (GS-US-367-1175)
Extrapolation, modelling and simulation studies	1	Study 5: Modelling and simulation study to leverage information gained in the SOF/VEL/GS-9857 adult development program to guide the most appropriate model to describe paediatric PK (SOF/VEL/GS-9857 Paediatric Exposures)
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 September 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes