EMA/114829/2017

European Medicines Agency decision

P/0063/2017

of 17 March 2017

on the acceptance of a modification of an agreed paediatric investigation plan for sofosbuvir / ledipasvir (Harvoni), (EMEA-001411-PIP01-12-M04) 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 European Medicines Agency's decision P/0248/2013 issued on 10 October 2013, the decision P/0181/2014 issued on 17 July 2014, the decision P/0003/2015 issued on 16 January 2015 and the decision P/0174/2016 issued on 30 June 2016,

Having regard to the application submitted by Gilead Sciences International Ltd. on 7 November 2016 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 27 January 2017, 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 sofosbuvir / ledipasvir (Harvoni), film-coated tablet, age-appropriate dosage form, other, age-appropriate oral solid dosage form, 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, Abington, CB21 6GT - Cambridge, United Kingdom.

EMA/PDCO/755962/2016
London, 27 January 2017

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

EMEA-001411-PIP01-12-M04

Scope of the application

Active substance(s):

Sofosbuvir / ledipasvir

Invented name:

Harvoni

Condition(s):

Treatment of chronic hepatitis C

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate dosage form, other

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Gilead Sciences International Ltd.

Information about the authorised medicinal product:

See Annex II

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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 7 November 2016 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/0248/2013 issued on 10 October 2013, the decision P/0181/2014 issued on 17 July 2014, the decision P/0003/2015 issued on 16 January 2015, and the decision P/0174/2016 issued on 30 June 2016.

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

The procedure started on 29 November 2016.

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 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.

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, age-appropriate dosage form, other, and age-appropriate oral solid dosage form, 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

Sofosbuvir (SOF) / ledipasvir (LDV) fixed dose combination (FDC) is indicated for the treatment of children 3 to less than 18 years of age with 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)

Age-appropriate dosage form, other

Age-appropriate oral solid dosage form

Film-coated tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of alternative age-appropriate oral solid dosage form for children 6 to less than 12 years of age and adolescents unable to swallow the adult tablet **Study 2** Development of age-appropriate dosage form for children 3 to less than 6 years of age

Non-clinical studies	0	Not applicable.
Clinical studies	3	**Study 3** Open-label, randomised, 2-period crossover, single-dose trial in healthy adults to evaluate relative bioavailability and safety of the age-appropriate paediatric formulation of sofosbuvir (SOF)/ledipasvir (LDV) fixed dose combination (FDC) versus the adult formulation **Study 4** Open-label, single-arm trial to evaluate pharmacokinetics, safety and efficacy of sofosbuvir (SOF)/ledipasvir (LDV) fixed-dose combination (FDC) and SOF/LDV FDC in combination with ribavirin (RBV) in children from 3 to less than 18 years of age with chronic hepatitis C genotype 1-6 infection **Study 5** Open-label, randomised, 2-period crossover, single-dose trial in healthy adults to evaluate relative bioavailability and safety of the age-appropriate paediatric formulation of sofosbuvir (SOF)/ledipasvir (LDV) fixed dose combination (FDC) versus the adult formulation
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 August 2018
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 chronic hepatitis C

Authorised indication(s):

- Harvoni is indicated for the treatment of chronic hepatitis C (CHC) in adults (see sections 4.2, 4.4 and 5.1).
- for hepatitis C virus (HCV) genotype-specific activity see sections 4.4 and 5.1.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use