EMA/779625/2014

European Medicines Agency decision

P/0002/2015

of 15 January 2015

on the acceptance of a modification of an agreed paediatric investigation plan for daclatasvir (dihydrochloride) / asunaprevir / (1aR,12bS)-8-Cyclohexyl-N-(dimethylsulfamoyl)-11-methoxy-1a-(((1R,5S)-3-methyl-3,8-diazabicyclo[3.2.1]oct-8-yl)carbonyl)-1,1a,2,12b-tetrahydrocyclopropa[d]indolo[2,1-a][2]benzazepine-5-carboxamide hydrochloride (BMS-791325) (EMEA-001485-PIP01-13-M01) 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

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on the acceptance of a modification of an agreed paediatric investigation plan for daclatasvir (dihydrochloride) / asunaprevir / (1aR,12bS)-8-Cyclohexyl-N-(dimethylsulfamoyl)-11-methoxy-1a-(((1R,5S)-3-methyl-3,8-diazabicyclo[3.2.1]oct-8-yl)carbonyl)-1,1a,2,12b-tetrahydrocyclopropa[d]indolo[2,1-a][2]benzazepine-5-carboxamide hydrochloride (BMS-791325) (EMEA-001485-PIP01-13-M01) 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/0182/2014 issued on 17 July 2014,

Having regard to the application submitted by Bristol-Myers Squibb International Corporation on 19 September 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 12 December 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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 daclatasvir (dihydrochloride) / asunaprevir / (1aR,12bS)-8-Cyclohexyl-N-(dimethylsulfamoyl)-11-methoxy-1a-(((1R,5S)-3-methyl-3,8-diazabicyclo[3.2.1]oct-8-yl)carbonyl)-1,1a,2,12b-tetrahydrocyclopropa[d]indolo[2,1-a][2]benzazepine-5-carboxamide hydrochloride (BMS-791325), age-appropriate dosage form, film-coated tablet, oral use, 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 Bristol-Myers Squibb International Corporation, Parc de l'Alliance, Avenue de Finlande 4, 1420 - Braine-l'Alleud, Belgium.

Done at London, 15 January 2015

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

EMA/PDCO/582107/2014

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

EMEA-001485-PIP01-13-M01

Scope of the application

Active substance(s):

Daclatasvir (dihydrochloride) / asunaprevir / (1aR,12bS)-8-Cyclohexyl-N-(dimethylsulfamoyl)-11-methoxy-1a-(((1R,5S)-3-methyl-3,8-diazabicyclo[3.2.1]oct-8-yl)carbonyl)-1,1a,2,12b-tetrahydrocyclopropa[d]indolo[2,1-a][2]benzazepine-5-carboxamide hydrochloride (BMS-791325)

Condition(s):

Treatment of chronic hepatitis C

Pharmaceutical form(s):

Age-appropriate dosage form

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bristol-Myers Squibb International Corporation

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb International Corporation submitted to the European Medicines Agency on 19 September 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/0182/2014 issued on 17 July 2014.

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

The procedure started on 14 October 2014.

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Scope of the modification

Some measures 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 in the scope set out in the Annex I of this opinion.

   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 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.

London, 12 December 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 chronic hepatitis C

The waiver applies to:

- the paediatric population from birth to less than 3 years of age;
- film-coated tablet and age-appropriate 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

Treatment of children and adolescents from 3 years to less than 18 years of age infected with genotype (GT)-1 or GT-4 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)

Age-appropriate dosage form

Film-coated tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Development of an age-appropriate dosage form
Non-clinical studies	4	**Study 2:** Pre- and postnatal development study with BMS-791325 **Study 3:** Ten-week Oral Toxicity Study of BMS-791325 in Juvenile Rats with a Five to Eight-Week Recovery **Study 4:** Pre- and postnatal development study with asunaprevir (ASV) **Study 5:** Ten-week Oral Toxicity Study of ASV in Juvenile Rats with a One-Month Recovery

Clinical studies	2	**Study 6:** Open-label, single-arm trial to evaluate pharmacokinetics (PK), safety, tolerability and efficacy of daclatasvir (DCV), asunaprevir (ASV) and BMS-791325 in combination in children from 3 to less than 18 years of age with chronic hepatitis C genotype (GT)-1b infection who are treatment-naïve. **Study 7:** Open-label, single-dose, randomised crossover study in healthy adult subjects to determine the bioavailability of the age-appropriate paediatric fixed-dose combination (FDC) formulation relative to the single agent tablets of ASV, DCV, and BMS-791325. **Study 8:** Open-label, single-arm trial to evaluate pharmacokinetics, safety, tolerability, efficacy and acceptability/palatability of the DCV/ASV/BMS-791325 fixed-dose combination (FDC) in children from 3 to less than 18 years of age with chronic hepatitis C GT1 or GT4 infection who are treatment-naïve or treatment-experienced
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 December 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes