



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/414575/2014

European Medicines Agency decision

P/0182/2014

of 17 July 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver 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) (EMA-001485-PIP01-13) 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 Bristol-Myers Squibb International Corporation on 7 June 2013 under Article 16(1) of Regulation (EC) No 1901/2006,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 20 June 2014, 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 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, 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 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, 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 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, 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 Bristol-Myers Squibb International Corporation, Parc de l'Alliance, Avenue de Finlande 4, 1420 - Braine-l'Alleud, Belgium.

Done at London, 17 July 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/206910/2014

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

EMA-001485-PIP01-13

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 16(1) of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb International Corporation submitted for agreement to the European Medicines Agency on 7 June 2013 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 17 July 2013.

Supplementary information was provided by the applicant on 28 March 2014. 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 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.

London, 20 June 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 One-Month 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