EMA/471499/2016

European Medicines Agency decision

P/0198/2016

of 15 July 2016

on the acceptance of a modification of an agreed paediatric investigation plan for (3-((4-Benzoyl-1-piperazinyl)(oxo)acetyl)-4-methoxy-7-(3-methyl-1H-1,2,4-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-1-yl)methyl dihydrogen phosphate, 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (BMS-663068) (EMEA-001687-PIP01-14-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

European Medicines Agency decision

P/0198/2016

of 15 July 2016

on the acceptance of a modification of an agreed paediatric investigation plan for (3-((4-Benzoyl-1-piperazinyl)(oxo)acetyl)-4-methoxy-7-(3-methyl-1H-1,2,4-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-1-yl)methyl dihydrogen phosphate, 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (BMS-663068) (EMEA-001687-PIP01-14-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/0258/2015 issued on 30 October 2015,

Having regard to the application submitted by Bristol-Myers Squibb International Corporation on 1 April 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 24 June 2016, 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 (3-((4-Benzoyl-1-piperazinyl)(oxo)acetyl)-4-methoxy-7-(3-methyl-1H-1,2,4-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-1-yl)methyl dihydrogen phosphate, 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (BMS-663068), prolonged-release tablet, prolonged-release granules, 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, B-1420 - Braine-l'Alleud, Belgium.

Done at London, 15 July 2016

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

EMA/PDCO/258791/2016
London, 24 June 2016

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

EMEA-001687-PIP01-14-M01

Scope of the application

Active substance(s):

(3-((4-Benzoyl-1-piperazinyl)(oxo)acetyl)-4-methoxy-7-(3-methyl-1H-1,2,4-triazol-1-yl)-1H-pyrrolo[2,3-c]pyridin-1-yl)methyl dihydrogen phosphate, 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (BMS-663068)

Condition(s):

Treatment of human immunodeficiency virus (HIV-1) infection

Pharmaceutical form(s):

Prolonged-release tablet

Prolonged-release granules

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 1 April 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/0258/2015 issued on 30 October 2015.

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

The procedure started on 26 April 2016.

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 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 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 human immunodeficiency virus (HIV-1) infection

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- prolonged-release tablet, prolonged-release granules, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition

Treatment of human immunodeficiency virus (HIV-1) infection

2.1.1. Indication(s) targeted by the PIP

Treatment of HIV-1 infection as part of a combination therapy in paediatric patients who have no more than 2 remaining available fully active antiretroviral therapies

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Prolonged-release tablet

Prolonged-release granules

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of a prolonged-release tablet **Study 2** Development of prolonged-release granules
Non-clinical studies	2	**Study 3** Oral pre- and postnatal development study in rats **Study 4** Ten-week oral toxicity study in juvenile rats with 8 weeks of recovery

Clinical studies	4	**Study 5** Open-label, single-arm trial to evaluate pharmacokinetics, safety, antiviral activity and acceptability/palatability of BMS-663068 in combination with optimised background therapy (OBT) in HIV-infected adolescents from 12 to less than 18 years of age who are failing their current combination antiretroviral therapy (cART) and have current or historical dual- or triple-class antiretroviral (ARV) resistance **Study 6** Open-label, two-stage, single-arm trial to evaluate pharmacokinetics, safety, antiviral activity and acceptability/palatability of BMS-663068 in combination with failing cART/OBT (Stage 1) or OBT only (Stage 2) in HIV-infected children from 2 to less than 12 years of age who are failing their current cART and have current or historical dual- or triple-class ARV resistance **Study 7** Open-label, randomised study in healthy adult volunteers to determine the bioavailability of the prolonged-release tablet developed in Study 1 relative to the adult prolonged-release tablet **Study 8** Open-label, randomised study in healthy adult volunteers to determine the bioavailability of the prolonged-release granules developed in Study 2 relative to the adult prolonged-release tablet
Extrapolation, modelling and simulation studies	2	**Study 9** Modelling and simulation study to support the use of the BMS-663068 in HIV-infected children and adolescents from 2 to less than 18 years of age who are failing their current cART and have current or historical dual- or triple-class ARV resistance **Study 10** Extrapolation study to support the use of the BMS-663068 in HIV-infected children and adolescents from 2 to less than 18 years of age who are failing their current cART and have current or historical dual- or triple-class ARV resistance
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 February 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes