EMA/182559/2014

European Medicines Agency decision

P/0090/2014

of 4 April 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for atazanavir / cobicistat (EMEA-001465-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 726/2004[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 application submitted by Bristol-Myers Squibb International Corporation on 6 May 2013 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 21 March 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 atazanavir / cobicistat, film-coated tablet, age-appropriate oral solid 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 atazanavir / cobicistat, film-coated tablet, age-appropriate oral solid 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 atazanavir / cobicistat, film-coated tablet, age-appropriate oral solid 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 Bristol-Myers Squibb International Corporation, Parc l'Alliance, Avenue de Finlande 4, 1420 Braine - l'Alleud, Belgium.

Done at London, 4 April 2014

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

EMA/PDCO/10596/2014

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

EMEA-001465-PIP01-13

Scope of the application

Active substance(s):

Atazanavir / cobicistat

Condition(s):

Treatment of HIV-1 infection

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral solid dosage form

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 6 May 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 12 June 2013.

Supplementary information was provided by the applicant on 19 December 2013. The applicant proposed modifications to the paediatric investigation plan.

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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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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, 21 March 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

1. Waiver

1.1. Condition: treatment of HIV-1 infection

The waiver applies to:

- The paediatric population from birth to less than 3 months of age;
- for film-coated tablet and age-appropriate oral solid dosage form, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: treatment of HIV-1 infection

2.1.1. Indication(s) targeted by the PIP

Treatment of human immunodeficiency virus (HIV-1) infected paediatric patients aged 3 months to less than 18 years of age in combination with other antiretroviral medicinal products

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

From 3 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	2	**Study 1** Development of film-coated tablet for use in adolescents weighing at least 40 kg **Study 2** Development of age-appropriate oral solid dosage form for use in paediatric population from 3 months to less than 18 years of age
Non-clinical studies	0	Not applicable.
Clinical studies	3	**Study 3** Open-label, randomised, crossover study in healthy adults to assess: • the bioequivalence of atazanavir (ATV) when co-administered with cobicistat (COBI) as a fixed dose combination (FDC) relative to the

Area	Number of studies	Description
		single agents following a light meal; • the relative bioavailability of COBI when administered with ATV as an FDC compared to co-administration of the single agents following a light meal; • the relative bioavailability of ATV and COBI when administered as an FDC compared to co-administration of the single agents under fasted conditions; • the effect of food (a light meal and a high fat meal) on the bioavailability of ATV and COBI in the FDC. **Study 4** Open-label, randomised, crossover study to obtain a preliminary estimate of the bioavailability of ATV and COBI when administered in prototype age-appropriate fixed-dose combination (FDC) formulation(s) to coadministration of the individual ATV and COBI age-appropriate formulations and to assess preliminary palatability/acceptability in healthy adults. **Study 5** Open-label, randomised, crossover study to evaluate the bioequivalence of atazanavir (ATV) and the bioavailability of cobicistat (COBI) in the age-appropriate oral solid dosage form in healthy adults when administered as a fixed dose combination (FDC) compared to: • the adult FDC tablet to support the use of the age appropriate FDC formulation in paediatric patients from 12 to less than 18 years of age; • the age-appropriate single agents to support the use of the age appropriate FDC formulation in children from 3 months to less than 18 years of age.
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 issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2019
Deferral for one or more measures contained in the paediatric investigation plan:	Yes