EMA/28175/2018

European Medicines Agency decision

P/0009/2018

of 30 January 2018

on the acceptance of a modification of an agreed paediatric investigation plan for atazanavir (sulphate) / cobicistat (Evotaz), (EMEA-001465-PIP01-13-M02) 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/0090/2014 issued on 4 April 2014 and the decision P/0181/2017 issued on 30 June 2017,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 25 September 2017 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 15 December 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 atazanavir (sulphate) / cobicistat (Evotaz), film-coated tablet, 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 Bristol-Myers Squibb Pharma EEIG, Uxbridge Park, Sanderson Road, UB8 1DH – Uxbridge, United Kingdom.

EMA/PDCO/659913/2017
London, 15 December 2017

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

EMEA-001465-PIP01-13-M02

Scope of the application

Active substance(s):

Atazanavir (sulphate) / cobicistat

Invented name:

Evotaz

Condition(s):

Treatment of human immunodeficiency virus (HIV-1) infection

Authorised indication(s):

See Annex II

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 Pharma EEIG

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb Pharma EEIG submitted to the European Medicines Agency on 25 September 2017 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/0090/2014 issued on 4 April 2014 and the decision P/0181/2017 issued on 30 June 2017.

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

The procedure started on 17 October 2017.

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.

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;
- film-coated tablet, age-appropriate oral solid dosage form, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

The waiver applies to:

- the paediatric population from 3 months to less than 3 years of age;
- film-coated tablet, age-appropriate oral solid dosage form, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of HIV-1 infection

2.1.1. Indication(s) targeted by the PIP

EVOTAZ is indicated in combination with other antiretroviral (ARV) medicinal products for the treatment of HIV-1 infected adults and children from 3 years of age without known mutations associated with resistance to atazanavir

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

From 3 years 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	1	**Study 1** Deleted during procedure EMEA-001465-PIP01-13-M01

		Study 2 Development of age-appropriate oral solid dosage form for use in paediatric population from 3 years 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 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 age-appropriate single agents to support the use of the age appropriate FDC formulation in children from 3 years 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/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2020
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 HIV-1 infection

Authorised indication(s):

- EVOTAZ is indicated in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults without known mutations associated with resistance to atazanavir

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use