EMA/21181/2023

European Medicines Agency decision

P/0027/2023

of 31 January 2023

on the acceptance of a modification of an agreed paediatric investigation plan for atazanavir (sulphate) / cobicistat (Evotaz), (EMEA-001465-PIP01-13-M05) 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 Union procedures for the authorisation and supervision of medicinal products for human 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, the decision P/0181/2017 issued on 30 June 2017, the decision P/0009/2018 of 30 January 2018, the decision P/0510/2020 issued on 22 December 2020 and the decision P/0041/2022 issued on 29 January 2022,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 8 September 2022 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 16 December 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

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, Plaza 254, Blanchardstown Corporate Park 2, D15 T867 - Dublin 15, Ireland.

EMA/773901/2022 Corr. 1 [1]
Amsterdam, 16 December 2022

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

EMEA-001465-PIP01-13-M05

Scope of the application

Active substance(s):

Atazanavir (sulphate) / cobicistat

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of human immunodeficiency virus (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 Pharma EEIG

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 8 September 2022 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, the decision P/0181/2017 issued on 30 June 2017, the decision P/0009/2018 of 30 January 2018, the decision P/0510/2020 issued on 22 December 2020 and the decision P/0041/2022 issued on 29 January 2022.

[1] 27 January 2023

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

The procedure started on 17 October 2022.

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 Paediatric Committee members of Liechtenstein and Norway 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 annexes 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 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 human immunodeficiency virus (HIV-1) infection

2.1.1. Indication(s) targeted by the PIP

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	Description
Quality-related studies	**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	Not applicable
Clinical studies	**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	Not applicable
Other studies	Not applicable
Other measures	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 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of human immunodeficiency virus (HIV-1) infection

Authorised indication(s):

- EVOTAZ is indicated in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults and adolescents (aged 12 years and older weighing at least 35 kg) without known mutations associated with resistance to atazanavir.
  - Invented name(s): EVOTAZ
  - Authorised pharmaceutical form(s): film-coated tablet
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure