EMA/950362/2022

European Medicines Agency decision

P/0551/2022

of 4 January 2023

on the acceptance of a modification of an agreed paediatric investigation plan for ceftazidime / avibactam (Zavicefta), (EMEA-001313-PIP01-12-M13) 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/0083/2013 issued on 26 April 2013, decision P/0133/2014 issued on 10 June 2014, decision P/0052/2015 issued on 6 March 2015, decision P/0251/2015 issued on 30 October 2015, decision P/0062/2017 issued on 17 March 2017, decision P/0314/2017 issued on 31 October 2017, decision P/0149/2018 issued on 17 May 2018, decision P/0340/2018 issued on 8 November 2018, decision P/0027/2021 issued on 27 January 2021, decision P/0001/2022 issued on 7 January 2022, and decision P/0258/2022 issued on 11 July 2022,

Having regard to the application submitted by Pfizer Europe MA EEIG on 9 September 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

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.

(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, 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 ceftazidime / avibactam (Zavicefta), powder for concentrate for solution for infusion, intravenous 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 Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 – Brussels, Belgium.

EMA/PDCO/771500/2022
Amsterdam, 16 December 2022

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

EMEA-001313-PIP01-12-M13

Scope of the application

Active substance(s):

Ceftazidime / avibactam

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of intra-abdominal infections

Treatment of urinary tract infections

Treatment of pneumonia

Treatment of infections due to aerobic Gram-negative organisms

Pharmaceutical form(s):

Powder for concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Pfizer Europe MA EEIG

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Pfizer Europe MA EEIG submitted to the European Medicines Agency on 9 September 2022 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0083/2013 issued on 26 April 2013, the decision P/0133/2014 issued on 10 June 2014, the decision P/0052/2015 issued on 6 March 2015, the decision P/0251/2015 issued on 30 October 2015, the decision P/0062/2017 issued on 17 March 2017, the decision P/0314/2017 issued on 31 October 2017,

the decision P/0149/2018 issued on 17 May 2018, the decision P/0340/2018 issued on 8 November 2018, the decision P/0027/2021 issued on 27 January 2021, the decision P/0001/2022 issued on 7 January 2022, and the decision P/0258/2022 issued on 11 July 2022.

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

The procedure started on 17 October 2022.

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 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 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

Not applicable

2. Paediatric investigation plan

2.1. Condition

Treatment of intra-abdominal infections

2.1.1. Indication(s) targeted by the PIP

Treatment of complicated intra-abdominal infections (cIAIs)

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** *This study was deleted as a result of procedure EMEA-001313-PIP01-12-M12.*
Non-clinical studies	**Study 2** 14-day repeat dose toxicity study in juvenile rats
Clinical studies	**Study 3 (D4280C00014)** Open-label, single dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from 3 months to less than 18 years of age with suspected or confirmed bacterial infection and receiving other systemic antibiotic therapy **Study 4 (C3591004)** Single-blind, randomised, active controlled, trial to evaluate safety, tolerability and efficacy of ceftazidime and avibactam in children from 3 months to less than 18 years of age with complicated intra-abdominal infections (cIAIs)

	Study 6 (C3591024) Open-label, single and multiple dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from birth to less than 3 months of age with suspected or confirmed infections due to aerobic Gram-negative pathogens requiring intravenous antibiotic treatment
Extrapolation, modelling and simulation studies	Not applicable
Other studies	Not applicable
Other measures	Not applicable

2.2. Condition

Treatment of urinary tract infections

2.2.1. Indication(s) targeted by the PIP

Treatment of complicated urinary tract infections (cUTIs)

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

2.2.4. Measures

Area	Description
Quality-related studies	**Study 1** *This study was deleted as a result of procedure EMEA-001313-PIP01-12-M12.*
Non-clinical studies	**Study 2** 14-day repeat dose toxicity study in juvenile rats *Same study as for condition "treatment of intra-abdominal infections"*
Clinical studies	**Study 3 (D4280C00014)** Open-label, single dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from 3 months to less than 18 years of age with suspected or confirmed bacterial infection and receiving other systemic antibiotic therapy *Same study as for condition "treatment of intra-abdominal infections"*

	Study 5 (C3591005) Single-blind, randomised, active controlled, trial to evaluate safety, tolerability and efficacy of ceftazidime and avibactam in children from 3 months to less than 18 years of age with complicated urinary tract infections (cUTI) **Study 6 (C3591024)** Open-label, single and multiple dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from birth to less than 3 months of age with suspected or confirmed infections due to Gram-negative pathogens requiring intravenous antibiotic treatment *Same study as for condition "treatment of intra-abdominal infections"*
Extrapolation, modelling and simulation studies	Not applicable
Other studies	Not applicable
Other measures	Not applicable

2.3. Condition

Treatment of pneumonia

2.3.1. Indication(s) targeted by the PIP

Treatment of nosocomial pneumonia

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

From birth to less than 18 years of age

2.3.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

2.3.4. Measures

Area	Description
Quality-related studies	**Study 1** *This study was deleted as a result of procedure EMEA-001313-PIP01-12-M12.*
Non-clinical studies	**Study 2** 14-day repeat dose toxicity study in juvenile rats *Same study as for condition "treatment of intra-abdominal infections"*

Clinical studies	**Study 3 (D4280C00014)** Open-label, single dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from 3 months to less than 18 years of age with suspected or confirmed bacterial infection and receiving other systemic antibiotic therapy *Same study as for condition "treatment of intra-abdominal infections"* **Study 6 (C3591024)** Open-label, single and multiple dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from birth to less than 3 months of age with suspected or confirmed infections due to Gram-negative pathogens requiring intravenous antibiotic treatment *Same study as for condition "treatment of intra-abdominal infections"* **Study 8 (C3591025)** *This study was deleted as a result of procedure 001313-PIP01-12-M10.*
Extrapolation, modelling and simulation studies	**Study 7 (CAZ-MS-PED-02)** Population pharmacokinetic (PK) modelling and PK/pharmacodynamic (PD) probability of target attainment (PTA) analysis for dose selection across paediatric age groups for patients with nosocomial pneumonia or with infections caused by Gram-negative bacteria **Study 9 (CAZ-MS-PED-04)** Extrapolation study of the clinical efficacy and safety data for ceftazidime-avibactam (CAZ-AVI) from the adult Phase III and paediatric programmes to paediatrics patients with nosocomial pneumonia or with infections caused by Gram-negative bacteria
Other studies	Not applicable
Other measures	Not applicable

2.4. Condition

2.4.1. Treatment of infections due to aerobic Gram-negative organisms

2.4.2. Indication(s) targeted by the PIP

Treatment of infections due to aerobic Gram-negative organisms in patients with limited treatment options

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

From birth to less than 18 years of age

2.4.4. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

2.4.5. Measures

Area	Description
Quality-related studies	**Study 1** *This study was deleted as a result of procedure EMEA-001313-PIP01-12-M12.*
Non-clinical studies	**Study 2** 14-day repeat dose toxicity study in juvenile rats *Same study as for condition "treatment of intra-abdominal infections"*
Clinical studies	**Study 3 (D4280C00014)** Open-label, single dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from 3 months to less than 18 years of age with suspected or confirmed bacterial infection and receiving other systemic antibiotic therapy *Same study as for condition "treatment of intra-abdominal infections"* **Study 6 (C3591024)** Open-label, single and multiple dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in children from birth to less than 3 months of age with suspected or confirmed infections due to Gram-negative pathogens requiring intravenous antibiotic treatment *Same study as for condition "treatment of intra-abdominal infections"*
Extrapolation, modelling and simulation studies	**Study 7 (CAZ-MS-PED-02)** Population pharmacokinetic (PK) modelling and PK/pharmacodynamic (PD) probability of target attainment (PTA) analysis for dose selection across paediatric age groups for patients with nosocomial pneumonia or with infections caused by Gram-negative bacteria *Same study as for condition "treatment of pneumonia"*

	Study 9 (CAZ-MS-PED-04) Extrapolation study of the clinical efficacy and safety data for ceftazidime-avibactam (CAZ-AVI) from the adult Phase III and paediatric programmes to paediatrics patients with nosocomial pneumonia or with infections caused by Gram-negative bacteria. Same study as for condition "treatment of pneumonia"
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 2023
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 intra-abdominal infections

Authorised indication(s):

- Treatment of complicated intra-abdominal infections (cIAI) in adults and paediatric patients aged 3 months and older
- Treatment of adult patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

2. Treatment of urinary tract infections

Authorised indication(s):

- Treatment of complicated urinary tract infection (cUTI), including pyelonephritis, in adults and paediatric patients aged 3 months and older
- Treatment of adult patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

3. Treatment of pneumonia

Authorised indication(s):

- Treatment of hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP), in adults and paediatric patients aged 3 months and older
- Treatment of adult patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

4. Treatment of infections due to aerobic Gram-negative organisms

Authorised indication(s):

- Infections due to aerobic Gram-negative organisms in adult patients and paediatric patients aged 3 months and older with limited treatment options

Authorised pharmaceutical form(s):

Powder for concentrate for solution for infusion (powder for concentrate)

Authorised route(s) of administration:

Intravenous use