MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100618-PIP01-22-M01

Scope of the Application

Active Substance(s)

AVIBACTAM; CEFTAZIDIME

Condition(s)

Treatment of intra-abdominal infections, Treatment of urinary tract infections, Treatment of pneumonia, Treatment of infections due aerobic Gram-negative organisms.

Pharmaceutical Form(s)

Powder for concentrate for solution for injection

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Pfizer Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Pfizer Limited submitted to the licensing authority on 18/07/2022 16:29 BST an application for a Modification

The procedure started on 16/01/2023 08:34 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100618-PIP01-22-M01

Of 06/03/2023 14:49 GMT

On the adopted decision for AVIBACTAM; CEFTAZIDIME (MHRA-100618-PIP01-22-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for AVIBACTAM; CEFTAZIDIME, Powder for concentrate for solution for injection , INTRAVENOUS USE .

This decision is addressed to Pfizer Limited, Ramsgate Road, Sandwich, UNITED KINGDOM, CT13 9NJ

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of intra-abdominal infections Condition 2: Treatment of urinary tract infections Condition 3: Treatment of pneumonia Condition 4: Treatment of infections due to aerobic Gram-negative organisms

2.2 Indication(s) targeted by the PIP:

Condition 1: For the treatment of complicated intra-abdominal infections (cIAIs) Condition 2: For the treatment of complicated urinary tract infections (cUTIs) Condition 3: For the treatment of nosocomial pneumonia Condition 4: For the treatment of infections due to aerobic Gram-negative organisms in patients with limited treatment options

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

For all 4 Conditions: All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

For all 4 Conditions: Powder for concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	(Same study for all 4 conditions) Study 1 Deleted during procedure MHRA-100618-PIP01-22-M01.
Non-Clinical Studies	1	(Same study for all 4 conditions) Study 2 14-day repeat dose toxicity study in juvenile rats.
Clinical Studies	4	(Same study for all 4 conditions) 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 for Condition 1 only) 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 for Condition 2 only) 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). (Same study for all 4 conditions) 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. (Study for Condition 3 only) Study 8 Deleted during procedure MHRA-100618-PIP01-22-M01.
Extrapolation, Modeling & Simulation Studies	2	(Same study for Conditions 3 and 4 only) 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 for Conditions 3 and 4 only) 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	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/09/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes