MHRA
10 South Colonnade
Canary Wharf
London
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United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (EMEA-001731-PIP01-14-M02) and to the deferral

MHRA-101246-PIP01-23-M01

Scope of the Application

Active Substance(s)

MEROPENEM; VABORBACTAM

Condition(s)

Treatment of Gram-negative bacterial infections

Pharmaceutical Form(s)

Powder for concentrate for solution for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Menarini International Operations Luxembourg S.A.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Menarini International Operations Luxembourg S.A. submitted to the licensing authority on 30/01/2024 13:30 GMT an application for a Modification

The procedure started on 15/03/2024 14:12 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-101246-PIP01-23-M01

Of 03/06/2024 13:10 BST

On the adopted decision for MEROPENEM; VABORBACTAM (MHRA-101246-PIP01-23-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 MEROPENEM; VABORBACTAM, Powder for concentrate for solution for infusion , INTRAVENOUS USE .

This decision is addressed to Menarini International Operations Luxembourg S.A., 1, Avenue de la Gare, Luxembourg, LUXEMBOURG, L-1611

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of Gram-negative bacterial infections

2.2 Indication(s) targeted by the PIP:

Treatment of complicated urinary tract infection (cUTI), including pyelonephritis.

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

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Powder for concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of age-appropriate formulation for intravenous use.
Non-Clinical Studies	2	Study 2 Dose-range finding study to support dose-selection for the main juvenile toxicity study and to determine maximum tolerated dose of combination. Study 3 Definitive juvenile toxicity study to assess toxicity of vaborbactam in combination with meropenem in juvenile animals and to evaluate delayed onset of toxicity and recovery from possible toxic effects during the recovery period.
Clinical Studies	3	Study 4 Open-label, single dose trial to evaluate pharmacokinetics, safety and tolerability study of meropenem in combination with vaborbactam in children from birth to less than 18 years of age with confirmed or suspected bacterial infections requiring intravenous antibiotics. Study 5 Study deleted during procedure MHRA-101246-PIP01-23-M01. Study 6 Open-label, multiple-dose, active controlled trial to evaluate pharmacokinetic, safety and tolerability study of meropenem in combination with vaborbactam in neonates from birth to less or equal than 90 days with late onset sepsis. Study 8 Study added during procedure MHRA-101246-PIP01-23-M01. Open label trial to evaluate

		pharmacokinetics, safety and efficacy of meropenem in combination with vaborbactam in children from 3 months to less than 18 years of age with complicated urinary tract infections (cUTI) including acute pyelonephritis (AP).
Extrapolation, Modeling & Simulation Studies	1	Study 7 Population PK/PD modelling and simulation study for dose selection across paediatric age groups for patients 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:	No
Date of completion of the paediatric investigation plan:	31/12/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes