

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

[gov.uk/mhra](https://www.gov.uk/mhra)

## **Decision Cover Letter**

### **Decision of the licensing authority to:**

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

MHRA-100690-PIP01-22-M01

### **Scope of the Application**

#### **Active Substance(s)**

IMIPENEM MONOHYDRATE; CILASTATIN SODIUM; RELEBACTAM MONOHYDRATE

#### **Condition(s)**

Treatment of infections caused by gram-negative organisms.

#### **Pharmaceutical Form(s)**

Powder for solution for infusion

#### **Route(s) of Administration**

INTRAVENOUS USE

#### **Name / Corporate name of the PIP applicant**

Merck Sharp and Dhome (UK) Limited

#### **Basis for the Decision**

Pursuant to the Human Medicines Regulations 2012, Merck Sharp and Dhome (UK) Limited submitted to the licensing authority on 22/11/2022 08:59 GMT an application for a Modification

The procedure started on 11/04/2023 07:47 BST

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.

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

[gov.uk/mhra](http://gov.uk/mhra)

## Final Decision Letter

MHRA-100690-PIP01-22-M01

Of 24/05/2023 16:31 BST

On the adopted decision for IMIPENEM MONOHYDRATE; CILASTATIN SODIUM; RELEBACTAM MONOHYDRATE (MHRA-100690-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 IMIPENEM MONOHYDRATE; CILASTATIN SODIUM; RELEBACTAM MONOHYDRATE, Powder for solution for infusion , INTRAVENOUS USE .

This decision is addressed to Merck Sharp and Dhome (UK) Limited, 120 Moorgate, LONDON, UNITED KINGDOM, EC2M 6UR

## ANNEX I

### 1. Waiver

#### 1.1 Condition:

Not applicable

### 2. Paediatric Investigation Plan:

#### 2.1 Condition(s):

Treatment of infections caused by gram-negative organisms

#### 2.2 Indication(s) targeted by the PIP:

Treatment of hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP) Treatment of bacterial infections caused by aerobic gram-negative organisms in patients with limited treatment options

### 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 solution for infusion

### 2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 Dose range-finding juvenile toxicity study. Study 2 Definitive juvenile toxicity study.
Clinical Studies	2	Study 3 (Ped001) Open-label study to evaluate the pharmacokinetics, safety and tolerability of a single dose of imipenem (monohydrate) / cilastatin (sodium) / relebactam (MK-7655A) and to identify the appropriate dose of MK-7655A in children from birth to less than 18 years of age with gram-negative bacterial infections. Study 4 (Ped002) Open-label, randomised, active-controlled trial to evaluate safety, tolerability and efficacy of MK-7655A in children from birth to less than 18 years of age with gram-negative bacterial infections. Study 5 was deleted during procedure EMEA-001809-PIP01-15-M01.
Extrapolation, Modeling & Simulation Studies	2	Study 6 (Modelling & Simulation Study) Modelling and simulation study to select doses in children from birth to less than 18 years of age with gram-negative bacterial infections. Study 7 (Extrapolation Study) Extrapolation study to evaluate the use of MK-7655A in the proposed paediatric indications in children from birth to less than 18 years of

		age with serious gram-negative bacterial infections.
<b>Other Studies</b>	0	Not applicable.
<b>Other Measures</b>	0	Not applicable.

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

<b>Concerns on potential long term safety and efficacy issues in relation to paediatric use:</b>	Yes
<b>Date of completion of the paediatric investigation plan:</b>	31/08/2024
<b>Deferral of one or more studies contained in the paediatric investigation plan:</b>	Yes