EMA/251740/2024

European Medicines Agency decision

P/0190/2024

of 14 June 2024

on the acceptance of a modification of an agreed paediatric investigation plan for imipenem (monohydrate) / cilastatin (sodium) / relebactam (MK-7655A) (Recarbrio), (EMEA-001809-PIP01-15-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/0163/2016 issued on 15 June 2016, the decision P/0173/2019 issued on 15 May 2019, the decision P/0279/2020 issued on 24 July 2020 and the decision P/0090/2023 issued on 10 March 2023,

Having regard to the application submitted by MSD Europe Belgium SRL on 18 January 2024 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 26 April 2024, 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 imipenem (monohydrate) / cilastatin (sodium) / relebactam (MK-7655A) (Recarbrio), powder for solution for infusion, parenteral 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 MSD Europe Belgium SRL, Boulevard du Souverain 25, 1170 – Brussels, Belgium.

EMA/PDCO/47454/2024
Amsterdam, 26 April 2024

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

EMEA-001809-PIP01-15-M05

Scope of the application

Active substance(s):

Imipenem (monohydrate) / cilastatin (sodium) / relebactam (MK-7655A)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of infections caused by gram-negative organisms

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Parenteral use

Name/corporate name of the PIP applicant:

MSD Europe Belgium SRL

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, MSD Europe Belgium SRL submitted to the European Medicines Agency on 18 January 2024 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0163/2016 issued on 15 June 2016, the decision P/0173/2019 issued on 15 May 2019, the decision P/0279/2020 issued on 24 July 2020 and the decision P/0090/2023 issued on 10 March 2023.

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

The procedure started on 26 February 2024.

Scope of the modification

Some measures and 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 member of Norway agrees 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 infections caused by gram-negative organisms

2.1.1. 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

2.1.2. 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 solution for infusion

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** Dose range-finding juvenile toxicity study **Study 2** Definitive juvenile toxicity study
Clinical studies	**Study 3 (PN020)** Open-label study to evaluate the pharmacokinetics, safety and tolerability of a single dose of imipenem/cilastatin/relebactam and to identify the appropriate dose of in children from birth to less than 18 years of age with gram-negative bacterial infections **Study 4 (PN021)** Open-label, randomised, active-controlled trial to evaluate safety, tolerability and efficacy imipenem/cilastatin/relebactam in children from birth to less

	than 18 years of age with gram-negative bacterial infections ***Study 5:*** *deleted during procedure EMEA-001809-PIP01-15-M01*
Extrapolation, modelling and simulation studies	**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 imipenem/cilastatin/relebactam in the proposed paediatric indications in children from birth to less than 18 years of age with serious gram-negative bacterial infections
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 December 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 infections caused by gram-negative organisms

– Authorised indication(s):

- Treatment of hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP), in adults (see sections 4.4 and 5.1).
  - Invented name(s): Recarbrio
  - Authorised pharmaceutical form(s): Powder for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure
- Treatment of bacteraemia that occurs in association with, or is suspected to be associated with HAP or VAP, in adults.
  - Invented name(s): Recarbrio
  - Authorised pharmaceutical form(s): Powder for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure
- Treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options (see sections 4.2, 4.4, and 5.1).
  - Invented name(s): Recarbrio
  - Authorised pharmaceutical form(s): Powder for solution for infusion
  - Authorised route(s) of administration: Intravenous use
  - Authorised via centralised procedure