EMA/365938/2020

European Medicines Agency decision

P/0267/2020

of 15 July 2020

on the acceptance of a modification of an agreed paediatric investigation plan for meropenem (trihydrate) / vaborbactam (Vaborem) (EMEA-001731-PIP01-14-M02) 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.

European Medicines Agency decision

P/0267/2020

of 15 July 2020

on the acceptance of a modification of an agreed paediatric investigation plan for meropenem (trihydrate) / vaborbactam (Vaborem) (EMEA-001731-PIP01-14-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0229/2015 issued on 22 October 2015,

Having regard to the application submitted by Menarini International Operations Luxembourg S.A. on 24 February 2020 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 29 May 2020, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for meropenem (trihydrate) / vaborbactam (Vaborem), powder for solution for infusion, intravenous 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 Menarini International Opernations Luxembourg S.A., 1, Avenue de la Gare, L-1611 - Luxembourg, Luxembourg.

EMA/PDCO/138351/2020 Corr
Amsterdam, 29 May 2020

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

EMEA-001731-PIP01-14-M02

Scope of the application

Active substance(s):

Meropenem (trihydrate) / vaborbactam

Invented name:

Vaborem

Condition(s):

Treatment of Gram-negative bacterial infections

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Menarini International Operations Luxembourg S.A.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Menarini International Operations Luxembourg S.A. submitted to the European Medicines Agency on 24 February 2020 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0229/2015 issued on 22 October 2015.

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

The procedure started on 31 March 2020.

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 Norwegian Paediatric Committee member 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 Gram-negative bacterial infections

2.1.1. Indication(s) targeted by the PIP

Treatment of complicated urinary tract infection (cUTI) including pyelonephritis

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	Number of studies	Description
Quality-related studies	1	**Study 1** Development of an 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 suspected or confirmed bacterial infections

		Study 5 Single blind, randomised, active controlled trial to evaluate pharmacokinetics, safety and efficacy of meropenem in combination with vaborbactam compared to standard of care in children from 3 months to less than 18 years of age with complicated urinary tract infections (cUTI) including acute pyelonephritis (AP) **Study 6** Open-label, randomised, 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
Extrapolation, modelling and 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 PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By October 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of infections

Authorised indication(s):

Vaborem is indicated for the treatment of the following infections in adults (see sections 4.4 and 5.1):

- Complicated urinary tract infection (cUTI), including pyelonephritis
- Complicated intra-abdominal infection (cIAI)
- Hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP).
- Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

Vaborem is also indicated for the treatment of infections due to aerobic Gram-negative organisms in

- adults with limited treatment options (see sections 4.2, 4.4 and 5.1).
- Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Authorised pharmaceutical form(s):

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

Authorised route(s) of administration:

Intravenous infusion