EMA/624853/2015

European Medicines Agency decision

P/0229/2015

of 22 October 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral for meropenem trihydrate (in combination with vaborbactam) (EMEA-001731-PIP01-14) 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 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 application submitted by Rempex Pharmaceuticals on 12 December 2014 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 September 2015, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a 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

A paediatric investigation plan for meropenem trihydrate (in combination with vaborbactam), powder for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for meropenem trihydrate (in combination with vaborbactam), powder for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Rempex Pharmaceuticals, 8 Sylvan Way, NJ 07054 – Parsippany, United States.

Done at London, 22 October 2015

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/448827/2015 corr
London, 11 September 2015

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral

EMEA-001731-PIP01-14

Scope of the application

Active substance(s):

Meropenem trihydrate (in combination with vaborbactam)

Condition(s):

Treatment of Gram-negative bacterial infections

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Rempex Pharmaceuticals

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Rempex Pharmaceuticals submitted for agreement to the European Medicines Agency on 12 December 2014 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 20 January 2015.

Supplementary information was provided by the applicant on 22 June 2015. The applicant proposed modifications to the paediatric investigation plan.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 annex 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.

Area	Number of studies	Description
		Study 5 Single blind, randomised, active controlled trial to evaluate pharmacokinetics, safety and efficacy of meropenem in combination with vaborbactam compared to piperacillin/tazobactam in children from 3 months to less than 18 years of age with complicated urinary tract infections (cUTI) including acute pyelonephritis (AP), and complicated intra-abdominal infections (cIAI). **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 March 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes