EMA/86510/2015

European Medicines Agency decision

P/0046/2015

of 6 March 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for eravacycline (EMEA-001555-PIP01-13) 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 Tetraphase Pharmaceuticals, Inc. on 11 October 2013 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 January 2015, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation, and Article 13 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 and on the granting of a waiver.

(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.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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 eravacycline, concentrate for solution for infusion, tablet, intravenous use, oral 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 eravacycline, concentrate for solution for infusion, tablet, intravenous use, oral 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

A waiver eravacycline, concentrate for solution for infusion, tablet, intravenous use, oral 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 4

This decision is addressed to Tetraphase Pharmaceuticals, Inc., 480 Arsenal Street, Suite 110, MA 02472100 – Watertown, United States.

Done at London, 6 March 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/676695/2014

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

EMEA-001555-PIP01-13

Scope of the application

Active substance(s):

Eravacycline

Condition(s):

Treatment of complicated intra-abdominal infection

Treatment of urinary tract infection

Pharmaceutical form(s):

Concentrate for solution for infusion

Tablet

Route(s) of administration:

Intravenous use

Oral use

Name/corporate name of the PIP applicant:

Tetraphase Pharmaceuticals, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Tetraphase Pharmaceuticals, Inc. submitted for agreement to the European Medicines Agency on 11 October 2013 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 19 November 2013.

Supplementary information was provided by the applicant on 27 October 2014. The applicant proposed modifications to the paediatric investigation plan.

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;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   The Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver 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.

London, 16 January 2015

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

1.1. Condition:

Treatment of complicated intra-abdominal infection

The waiver applies to:

- the paediatric population from birth to less than 8 years of age;
- concentrate for solution for infusion, intravenous use and tablet, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1.2. Condition:

Treatment of urinary tract infection

The waiver applies to:

- the paediatric population from birth to less than 8 years of age;
- concentrate for solution for infusion, intravenous use, and tablet, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Treatment of complicated intra-abdominal infection

2.1.1. Indication(s) targeted by the PIP

Complicated intra-abdominal infection.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 8 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

Tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1: Development of tablets appropriate to the paediatric population.
Non-clinical studies	2	Study 2: Definitive juvenile toxicity study to determine the toxicity of eravacycline following multiple dose administrations by intravenous injection to juvenile rats. Study 3: Reprotox: (enhanced) pre- and post-natal development study to evaluate toxicity of eravacycline in F1 generation rats following intravenous administration of eravacycline to F0 dams during pregnancy and lactation.
Clinical studies	2	Study 4: Open-label, multiple dose trial to evaluate pharmacokinetics and safety of eravacycline in children from 8 to less than 18 years of age with suspected or confirmed bacterial infection. Study 5: Double-blind, randomised, single dose, active controlled trial to evaluate safety of eravacycline compared to ertapenem in children with complicated intra-abdominal infections and to cefepime in children with complicated urinary tract infections from 8 to less than 18 years of age.
Extrapolation, modelling and simulation studies	2	Study 6: PK-PD modelling and simulation study to optimize paediatric dosing of eravacycline for studies 4 and 5. Study 7: Extrapolation study to evaluate the use of eravacycline in children from 8 to less than 12 years of age with complicated intra-abdominal infections or with complicated urinary tract infections, using data from the literature and data gathered in the adult clinical development program.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of urinary tract infection

2.2.1. Indication(s) targeted by the PIP

Complicated urinary tract infection.

2.2.2. Subset(s) of the paediatric population concerned by the paediatric development

From 8 to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Concentrate for solution for infusion

Tablet

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	1	Study 1: Development of tablets appropriate to the paediatric population (same measure as for Treatment of complicated intra-abdominal infection).
Non-clinical studies	2	Study 2: Definitive juvenile toxicity study to determine the toxicity of eravacycline following multiple dose administrations by intravenous injection to juvenile rats (same measure as for Treatment of complicated intra-abdominal infection). Study 3: Reprotox: (enhanced) pre- and post-natal development study to evaluate toxicity of eravacycline in F1 generation rats following intravenous administration of eravacycline to F0 dams during pregnancy and lactation (same measure as for Treatment of complicated intra-abdominal infection).
Clinical studies	2	Study 4: Open-label, multiple dose trial to evaluate pharmacokinetics and safety of eravacycline in children from 8 to less than 18 years of age with suspected or confirmed bacterial infection (same measure as for Treatment of complicated intra-abdominal infection). Study 5: Double-blind, randomised, single dose, active controlled trial to evaluate safety of eravacycline compared to ertapenem in children with complicated intra-abdominal infections and to cefepime in children with complicated urinary tract infections from 8 to less than 18 years of age (same measure as for Treatment of complicated intra-abdominal infection).
Extrapolation, modelling and simulation studies	2	Study 6: PK-PD modelling and simulation study to optimize paediatric dosing of eravacycline for studies 4 and 5 (same measure as for Treatment of complicated intra-abdominal infection). Study 7: Extrapolation study to evaluate the use of eravacycline in children from 8 to less than 12 years of age with complicated intra-abdominal infections or with complicated urinary tract infections, using data from the literature and data gathered in the adult clinical development program (same measure as for Treatment of complicated intra-abdominal infection).

Area	Number of measures	Description
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:	Yes
Date of completion of the paediatric investigation plan:	By December 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes