EMA/765277/2016 corr

# European Medicines Agency decision

P/0336/2016

of 2 December 2016

on the acceptance of a modification of an agreed paediatric investigation plan for eravacycline (EMEA-001555-PIP01-13-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.**

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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 European Medicines Agency's decision P/0046/2015 issued on 6 March 2015,

Having regard to the application submitted by Tetraphase Pharmaceuticals, Inc. on 25 July 2016 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 14 October 2016, 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 and to the waiver.

(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 and to the 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***

Changes to the agreed paediatric investigation plan for eravacycline, powder for concentrate for solution for infusion, tablet, age-appropriate oral formulation, intravenous use, oral use, including changes to the deferral and to the waiver, 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 Tetraphase Pharmaceuticals, Inc., 480 Arsenal Street, Suite 110, MA - 02472, Watertown, USA.

EMA/PDCO/515526/2016 Corr
London, 14 October 2016

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

EMEA-001555-PIP01-13-M02

## Scope of the application

**Active substance(s):**

Eravacycline

**Condition(s):**

Treatment of complicated intra-abdominal infection

Treatment of urinary tract infection

**Pharmaceutical form(s):**

Powder for concentrate for solution for infusion

Tablet

Age-appropriate oral formulation

**Route(s) of administration:**

Intravenous use

Oral use

**Name/corporate name of the PIP applicant:**

Tetraphase Pharmaceuticals, Inc.

## Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Tetraphase Pharmaceuticals, Inc. submitted to the European Medicines Agency on 25 July 2016 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0046/2015 issued on 6 March 2015.

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

The procedure started on 16 August 2016.

## Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A waiver for a new pharmaceutical form has been added.

## 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 and to the waiver 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 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 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

## *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;
- powder for concentrate for solution for infusion, intravenous use and tablet, oral use and age-appropriate oral formulation, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

And to:

- the paediatric population from 8 to less than 18 years of age;
- tablet, oral use and age-appropriate oral formulation, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

## *1.2. Condition:*

Treatment of urinary tract infection

The waiver applies to:

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

And to:

- the paediatric population from 8 to less than 18 years of age;
- tablet, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

# 2. Paediatric investigation plan

## *2.1. Condition: Treatment of complicated intra-abdominal infection*

### 2.1.1. Indication(s) targeted by the PIP

Treatment of 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)

Powder for concentrate for solution for infusion

### 2.1.4. Measures

| Area | Number of measures | Description |
|---|---|---|
| Quality-related studies | 0 | Study 1:<br>This study was deleted as a result of procedure EMEA-001555-PIP01-13-M02. |
| Non-clinical studies | 2 | Study 2:<br>Definitive juvenile toxicity study to determine the toxicity of eravacycline following multiple dose administrations by intravenous injection to juvenile rats.<br>Study 3:<br>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:<br>Open-label single dose trial to evaluate pharmacokinetics and safety of intravenous (IV) eravacycline in children from 8 to less than 18 years of age with suspected or confirmed bacterial infection and receiving other systemic antibiotic therapy.<br>Study 5:<br>Double-blind, randomised, IV dose, active controlled trial to evaluate safety of intravenous (IV) eravacycline compared to ertapenem in children with complicated intra-abdominal infections from 8 to less than 18 years of age. |

| | | |
|---|---|---|
| Extrapolation, modelling and simulation studies | 2 | Study 6:<br>PK-PD modelling and simulation study to optimise paediatric dosing of eravacycline for studies 4 (TP-434-028), 5 (TP-434-029), 8 (TP-434-030) and 9 (TP-434-031).<br>Study 7:<br>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

Treatment of 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)

Powder for concentrate for solution for infusion

Age-appropriate oral formulation

### 2.2.4. Measures

| **Area** | **Number of measures** | **Description** |
|---|---|---|
| Quality-related studies | 1 | Study 1:<br>Development of an age-appropriate oral formulation for the paediatric population. |
| Non-clinical studies | 2 | Study 2:<br>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).<br>Study 3:<br>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:<br><br>This study was deleted as a result of procedure EMEA-001555-PIP01-13-M02.Study 5 (TP-434-029):<br><br>This study was deleted as a result of procedure EMEA-001555-PIP01-13-M02.<br><br>Study 8:<br><br>Open-label trial to evaluate pharmacokinetics and safety of a single intravenous (IV) dose of eravacycline followed by multiple oral doses in children from 8 to less than 18 years of age with suspected or confirmed bacterial infection and receiving other systemic antibiotic therapy.<br><br>Study 9:<br><br>Double-blind, randomised, active controlled trial to evaluate safety of intravenous (IV) followed by oral eravacycline compared 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:<br><br>PK-PD modelling and simulation study to optimise paediatric dosing of eravacycline for studies 4 (TP-434-028), 5 (TP-434-029), 8 (TP-434-030) and 9 (TP-434-031) (same measure as for Treatment of complicated intra-abdominal infection).<br><br>Study 7:<br><br>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). |
| 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 June 2026 |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |