EMA/631366/2019

European Medicines Agency decision

P/0420/2019

of 4 December 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for iclaprim (mesylate) (EMEA-002391-PIP02-19) 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 Hemex Germany GmbH on 21 January 2019 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 18 October 2019, in accordance with Article 17 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 iclaprim (mesylate), concentrate 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 iclaprim (mesylate), concentrate 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 Motif Bio plc, 201 Temple Chambers, 3-7 Temple Avenue, EC4Y - 0DT London, United Kingdom.

EMA/PDCO/125885/2019
Amsterdam, 18 October 2019

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

EMEA-002391-PIP02-19

Scope of the application

Active substance(s):

Iclaprim (mesylate)

Condition(s):

Treatment of acute bacterial skin and skin structure infections

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Motif Bio plc

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Hemex Germany GmbH submitted for agreement to the European Medicines Agency on 21 January 2019 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 26 February 2019.

Supplementary information was provided by the applicant on 13 May 2019. The applicant proposed modifications to the paediatric investigation plan.

On 27 September 2019 Hemex Germany GmbH requested to transfer the paediatric investigation plan to Motif Bio plc.

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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 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

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 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 acute bacterial skin and skin structure infections

2.1.1. Indication(s) targeted by the PIP

Treatment of acute bacterial skin and skin structure infections

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)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age appropriate ethanol-free pharmaceutical form for intravenous use
Non-clinical studies	3	**Study 2** Preliminary study in juvenile rats to determine the tolerability (including local irritation) and feasibility (doses / volumes) of parenteral administration of the ethanol-free iclaprim formulation, to decide on the suitability of this route for the Juvenile Tox Study 2 and Juvenile Tox Study 3 **Study 3** Dose range-finding juvenile toxicity study in rats to determine the tolerability and toxicokinetics of a range of dosage levels of ethanol-free iclaprim formulation **Study 4** Definitive juvenile toxicity study to determine the effects of iclaprim over the entire period of critical brain development to maturation

Clinical studies	4	**Study 5** Open-label, single-dose study to evaluate the pharmacokinetics, tolerability and safety of IV ethanol-free iclaprim in paediatric patients from 12 months to less than 18 years of age with suspected or proven infections caused by Gram-positive bacteria who are concurrently receiving standard antibiotic IV therapy **Study 6** Open-label, single-dose study to evaluate the pharmacokinetics, tolerability and safety of IV ethanol-free iclaprim in paediatric patients from birth to less than 12 months of age with suspected or proven infections caused by Gram-positive bacteria who are concurrently receiving standard antibiotic IV therapy **Study 7** Randomised, investigator-blinded, comparative study to assess the safety and efficacy of IV ethanol-free iclaprim in paediatric subjects from birth to less than 24 months of age with proven or suspected acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive organisms **Study 8** Single centre, open-label, single-dose, crossover trial to evaluate the bioequivalence of IV ethanol-free iclaprim vs ethanol-containing iclaprim formulation in healthy adult subjects
Extrapolation, modelling and simulation studies	2	**Study 9** Population PK-PD modelling and simulation study to evaluate the use of IV ethanol free iclaprim in paediatric patients from birth to less than 18 years of age **Study 10** Extrapolation study of the clinical safety and efficacy of ethanol-free iclaprim to children from birth to less than 18 years of age with acute bacterial skin and skin structure infections (ABSSSI)
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 February 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes