EMA/170148/2019

European Medicines Agency decision

P/0066/2019

of 22 March 2019

on the acceptance of a modification of an agreed paediatric investigation plan for lefamulin (EMEA-002075-PIP01-16-M01) 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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on the acceptance of a modification of an agreed paediatric investigation plan for lefamulin (EMEA-002075-PIP01-16-M01) 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/0241/2017 issued on 4 September 2017,

Having regard to the application submitted by Nabriva Therapeutics AG on 25 October 2018 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 1 February 2019, 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 lefamulin, concentrate for solution for infusion, coated tablet, age-appropriate oral solid dosage form, intravenous use, oral 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 Nabriva Therapeutics AG, Leberstrasse 20, A-1110 - Vienna, Austria.

EMA/PDCO/798100/2018
London, 1 February 2019

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

EMEA-002075-PIP01-16-M01

Scope of the application

Active substance(s):

Lefamulin

Condition(s):

Treatment of community-acquired pneumonia

Pharmaceutical form(s):

Concentrate for solution for infusion

Coated tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Intravenous use

Oral use

Name/corporate name of the PIP applicant:

Nabriva Therapeutics AG

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Nabriva Therapeutics AG submitted to the European Medicines Agency on 25 October 2018 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0241/2017 issued on 4 September 2017.

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

The procedure started on 4 December 2018.

Scope of the modification

Some 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 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 community-acquired pneumonia

2.1.1. Indication(s) targeted by the PIP

Treatment of community-acquired pneumonia

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

Coated tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of age-appropriate oral solid dosage form for use in children birth to less than 12 years of age
Non-clinical studies	5	**Study 2** Pharmacokinetic and tolerability dose range finding juvenile toxicity study in Sprague-Dawley rat testing the oral, intravenous (IV) and subcutaneous (SC) route **Study 3** Pre- and post-natal development study via intravenous route in the rat **Study 4** Pharmacokinetic and tolerability dose range finding juvenile toxicity study in Sprague-Dawley rat testing the oral route **Study 5** *In vitro* protein binding in plasma of paediatric subjects using equilibrium dialysis to determine the *in vitro* plasma protein binding of different age groups

		Study 6 Repeated dose toxicity study in juvenile Sprague-Dawley rats
Clinical studies	4	**Study 7** Open-label, randomised, crossover study to evaluate the absolute and relative bioavailability and pharmacokinetics (PK) of a 600 mg oral paediatric formulation of lefamulin in comparison to lefamulin 150 mg administered intravenously and 600 mg IR tablet administered orally in healthy adult volunteers **Study 8** Open-label, non-controlled trial to evaluate PK and safety of intravenous lefamulin in children from birth to less than 18 years of age with suspected or confirmed bacterial infection **Study 9** Open-label, non-controlled trial to evaluate PK and safety of oral lefamulin in children from birth to less than 18 years of age with suspected or confirmed bacterial infection **Study 10** Open-label, randomised, active-control trial to evaluate safety, pharmacokinetics and efficacy of lefamulin in children from 2 months to less than 18 years of age with community-acquired bacterial pneumonia (CABP)
Extrapolation, modelling and simulation studies	3	**Study 11** Population PK model to establish the appropriate dose of lefamulin in children in Study 8 and Study 9 **Study 12** PK / PD model to confirm the appropriate dose of lefamulin in children less than 2 years of age in Part B of Study 8 and Study 9 **Study 13** Update of population PK model after Study 10 with confirmation of dose recommendations for lefamulin in paediatric patients with suspected or confirmed bacterial 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:	No
Date of completion of the paediatric investigation plan:	By December 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes