

EMA/507360/2017

European Medicines Agency decision

P/0241/2017

of 4 September 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral for lefamulin (EMEA-002075-PIP01-16) 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.

European Medicines Agency decision

P/0241/2017

of 4 September 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral for lefamulin (EMA-002075-PIP01-16) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Nabriva Therapeutics AG on 28 November 2016 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 21 July 2017, 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 lefamulin, concentrate for solution for infusion, coated tablet, age-appropriate oral solid dosage form, 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 lefamulin, concentrate for solution for infusion, coated tablet, age-appropriate oral solid dosage form, 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

This decision is addressed to Nabriva Therapeutics AG, Leberstrasse 20, A-1110 - Vienna, Austria.

EMA/PDCO/288718/2017

London, 21 July 2017

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

EMA-002075-PIP01-16

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 16(1) of Regulation (EC) No 1901/2006 as amended, Nabriva Therapeutics AG submitted for agreement to the European Medicines Agency on 28 November 2016 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 3 January 2017.

Supplementary information was provided by the applicant on 20 April 2017. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

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 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 <i>In vitro</i> protein binding in plasma of paediatric subjects using equilibrium dialysis to determine the <i>in vitro</i> 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 March 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes