EMA/131048/2016

European Medicines Agency decision

P/0075/2016

of 18 March 2016

on the acceptance of a modification of an agreed paediatric investigation plan for naloxone (hydrochloride) (EMEA-001567-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/0305/2014 issued on 24 November 2014 and the decision P/0219/2015 issued on 2 October 2015,

Having regard to the application submitted by Develco Pharma GmbH on 9 November 2015 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 29 January 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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 naloxone (hydrochloride), prolonged-release tablet, age-appropriate prolonged-release oral formulation, oral use, 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 Develco Pharma GmbH, Grienmatt 42, 79650 – Schopfheim, Germany.

Done at London, 18 March 2016

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/748258/2015
London, 29 January 2016

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

EMEA-001567-PIP01-13-M02

Scope of the application

Active substance(s):

Naloxone (hydrochloride)

Condition(s):

Treatment of opioid-induced constipation

Pharmaceutical form(s):

Prolonged-release tablet

Age-appropriate prolonged-release oral formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Develco Pharma GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Develco Pharma GmbH submitted to the European Medicines Agency on 9 November 2015 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/0305/2014 issued on 24 November 2014 and the decision P/0219/2015 issued on 2 October 2015.

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

The procedure started on 30 November 2015.

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Scope of the modification

Some measures and 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 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 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

1.1. Condition

Treatment of opioid-induced constipation

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- prolonged-release tablet, age-appropriate prolonged-release oral formulation, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of opioid-induced constipation

2.1.1. Indication(s) targeted by the PIP

Treatment of opioid-induced constipation

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

From 2 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Prolonged-release tablet

Age-appropriate prolonged-release oral formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate prolonged-release oral formulation.
Non-clinical studies	0	Not applicable.
Clinical studies	3	**Study 2** Open-label, multiple dose, uncontrolled trial to evaluate steady-state pharmacokinetics of naloxone in children from 6 to less than 12 years of age with opioid-induced constipation.

		Study 3 Open-label, single dose, comparative bioavailability trial to evaluate the age-appropriate naloxone prolonged-release oral formulation in comparison to naloxone prolonged-release tablets in healthy adults. **Study 4** Open-label, multiple-dose, uncontrolled trial to evaluate pharmacokinetics and safety of naloxone in children from 2 to less than 6 years of age with opioid-induced constipation.
Extrapolation, modelling and simulation studies	1	**Study 5** Extrapolation study to evaluate the use of naloxone in the treatment of opioid-induced constipation in children from 12 to less than 18 years of age with opioid-induced constipation.
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 June 2021
Deferral for one or more measures contained in the paediatric investigation plan:	Yes