EMA/643802/2014

European Medicines Agency decision

P/0305/2014

of 24 November 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for naloxone (hydrochloride) (EMEA-001567-PIP01-13) 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 Develco Pharma GmbH on 10 October 2013 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 10 October 2014, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 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 and on the granting of a waiver.

(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.

(4) It is therefore appropriate to adopt a decision granting a 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

A paediatric investigation plan for naloxone (hydrochloride), prolonged-release tablet, age-appropriate prolonged-release oral formulation, 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 naloxone (hydrochloride), prolonged-release tablet, age-appropriate prolonged-release oral formulation, 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

A waiver for naloxone (hydrochloride), prolonged-release tablet, age-appropriate prolonged-release oral formulation, 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 4

This decision is addressed to Develco Pharma GmbH, Grienmatt 42, 79650 – Schopfheim, Germany.

Done at London, 24 November 2014

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

EMA/PDCO/452960/2014

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

EMEA-001567-PIP01-13

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 16(1) of Regulation (EC) No 1901/2006 as amended, Develco Pharma GmbH submitted for agreement to the European Medicines Agency on 10 October 2013 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 19 November 2013.

Supplementary information was provided by the applicant on 21 July 2014. The applicant proposed modifications to the paediatric investigation plan.

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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 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   The Icelandic and 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 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.

London, 10 October 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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