EMA/592453/2014

European Medicines Agency decision

P/0283/2014

of 30 October 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver for landiolol (hydrochloride) (EMEA-001150-PIP02-13) 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 AOP Orphan Pharmaceuticals AG on 13 December 2013 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 12 September 2014, 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 and on the refusal 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 refusing 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 landiolol (hydrochloride), powder for solution for infusion, concentrate for solution for injection, 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 landiolol (hydrochloride), powder for solution for infusion, concentrate for solution for injection, 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

A waiver for landiolol (hydrochloride), powder for solution for infusion, concentrate for solution for injection, 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 refused.

Article 4

This decision is addressed to AOP Orphan Pharmaceuticals AG, Wilhelminenstrasse 91/IIf, A-1160 – Vienna, Austria.

Done at London, 30 October 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/592453/2014 Corr

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

EMEA-001150-PIP02-13

Scope of the application

Active substance(s):

Landiolol (hydrochloride)

Condition(s):

Treatment of supraventricular arrhythmias

Prevention of supraventricular arrhythmias

Pharmaceutical form(s):

Powder for solution for infusion

Concentrate for solution for injection

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

AOP Orphan Pharmaceuticals AG

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AOP Orphan Pharmaceuticals AG submitted for agreement to the European Medicines Agency on 13 December 2013 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 21 January 2014.

Supplementary information was provided by the applicant on 23 June 2014. The applicant proposed modifications to the paediatric investigation plan and requested a waiver under Article 13 of said Regulation.

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 refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population and the above mentioned conditions as it does not meet the grounds detailed in Article 11(1) of said Regulation.

   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 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, 12 September 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

Prevention of supraventricular arrhythmias

The request for the waiver applied to:

- all subsets of the paediatric population from birth to less than 18 years of age
- powder for solution for infusion and concentrate for solution for injection for intravenous use
- on the grounds that the specific medicinal product is likely to be unsafe.

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (a) the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;
- (b) the disease or condition for which the specific medicinal product is intended occurs only in adult populations;
- (c) the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Because:

- the PDCO disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe;
- the disease or condition for which the specific medicinal product is intended, does occur in the paediatric population(s);
- measures would be justified by the expected therapeutic benefit and clinical trials may be feasible;
- the specific medicinal product may represent a significant therapeutic benefit as the needs are not met;
- clinical studies may fulfil a therapeutic need of the paediatric population.

The waiver request is therefore refused by the PDCO.

1.2. Condition

Treatment of supraventricular arrhythmias

The request for the waiver applied to:

- preterm and term newborn infants from birth to less than 28 days of age;
- powder for solution for infusion and concentrate for solution for injection for intravenous use;
- on the grounds that the specific medicinal product is likely to be unsafe.

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (a) the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;

- (b) the disease or condition for which the specific medicinal product is intended occurs only in adult populations;
- (c) the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

Because:

- the PDCO disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe;
- the disease or condition for which the specific medicinal product is intended, does occur in the paediatric population(s);
- measures would be justified by the expected therapeutic benefit and clinical trials may be feasible;
- the specific medicinal product may represent a significant therapeutic benefit as the needs are not met;
- clinical studies may fulfil a therapeutic need of the paediatric population.

The waiver request is therefore refused by the PDCO.

2. Paediatric investigation plan

2.1. Condition

Treatment of supraventricular arrhythmias

2.1.1. Indication(s) targeted by the PIP

Treatment of supraventricular tachyarrhythmias

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)

Powder for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of powder for solution suitable for paediatric use.
Non-clinical studies	0	Not applicable.

Clinical studies	1	**Study 2** Multicentre open-label uncontrolled study to investigate the effectiveness and safety of landiolol in controlling supraventricular tachycardia including inappropriate sinus tachycardia, junctional ectopic tachycardia, atrial flutter, atrial fibrillation, focal atrial tachycardia; and atrioventricular nodal re-entry tachycardia and atrioventricular reciprocating (re-entry) tachycardia refractory to treatment with adenosine in surgical (peri- and postoperative, cardiac and non-cardiac surgery) and non- surgical paediatric patients.
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition

Prevention of supraventricular arrhythmias

2.2.1. Indication(s) targeted by the PIP

Prevention of supraventricular tachyarrhythmias

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

From birth to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Powder for solution for infusion

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of powder for solution suitable for paediatric use.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 3** Open-label uncontrolled study to investigate the effectiveness and safety of landiolol in preventing

		supraventricular tachycardia in paediatric patients undergoing cardiac surgery.
Extrapolation, modelling and simulation studies	0	Not applicable.
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 July 2018
Deferral for one or more measures contained in the paediatric investigation plan:	Yes