

EMA/584824/2018

European Medicines Agency decision

P/0289/2018

of 12 September 2018

on the agreement of a paediatric investigation plan and on the granting of a waiver for palovarotene (EMEA-001662-PIP03-17) 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 726/2004¹,

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 Clementia Pharmaceuticals Inc. on 22 January 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 27 July 2018, in accordance with Article 17 of Regulation (EC) No 1901/2006 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 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 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 palovarotene, capsule, hard, 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 waiver for palovarotene, capsule, hard, 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 Clementia Pharmaceuticals Inc., 4150 Ste-Catherine Street West, Suite 550, H3Z 2Y5 - Montreal, Canada.

EMA/PDCO/302104/2018 **Corr**

London, 27 July 2018

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

EMA-001662-PIP03-17

Scope of the application

Active substance(s):

Palovarotene

Condition(s):

Treatment of multiple osteochondromas

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name / corporate name of the PIP applicant:

Clementia Pharmaceuticals Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Clementia Pharmaceuticals Inc. submitted for agreement to the European Medicines Agency on 22 January 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 27 February 2018.

Supplementary information was provided by the applicant on 7 May 2018. The applicant proposed modifications to the paediatric investigation plan.

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 17(1) 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 and Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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 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 multiple osteochondromas

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- capsule, hard, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe;

and to:

- the paediatric population from 15 years to less than 18 years of age with closed epiphyses;
- capsule, hard, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition

Treatment of multiple osteochondromas

2.1.1. Indication(s) targeted by the PIP

Treatment of multiple osteochondromas

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

From 2 years to less than 15 years of age with open epiphyses

2.1.3. Pharmaceutical form(s)

Capsule, hard

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	Study 1 (9000317) Dose range-finding study to evaluate the toxicity of palovarotene in rats 1, 2, or 3 weeks old.

		Study 2 (6700132) Juvenile toxicity study to evaluate the toxicity and reversibility of effects after palovarotene administration in 3- to 9-week-old rats.
Clinical studies	2	Study 3 (PVO-2A-201) Double-blind, randomised, double dose, placebo controlled trial to compare the efficacy of palovarotene with placebo in preventing the formation of new osteochondromas in children from 2 years to less than 15 years of age with open epiphyses with multiple osteochondromas due to exostosin 1 (Ext1) or exostosin 2 (Ext2) mutations. Study 4 (PVO-2A-301) Double-blind, randomised, single dose, placebo controlled trial to compare the efficacy of palovarotene with placebo in preventing the formation of new osteochondromas in children from 2 years to less than 15 years of age with open epiphyses with multiple osteochondromas due to exostosin 1 (Ext1) or exostosin 2 (Ext2) mutations.
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:	Yes
Date of completion of the paediatric investigation plan:	By August 2026
Deferral for one or more measures contained in the paediatric investigation plan:	No