EMA/649951/2021

European Medicines Agency decision

P/0562/2021

of 31 December 2021

on the acceptance of a modification of an agreed paediatric investigation plan for palovarotene (EMEA-001662-PIP01-14-M05) 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/0127/2015 issued on 5 June 2015, the decision P/0364/2017 issued on 1 December 2017, the decision P/0121/2018 issued on 11 April 2018, the decision P/0144/2020 issued on 15 April 2020 and the decision P/0441/2020 issued on 1 December 2020,

Having regard to the application submitted by Ipsen Pharma on 6 August 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 12 November 2021, in accordance with Article 22 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 acceptance of changes to the agreed paediatric investigation plan and on the refusal of a waiver.

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

(3) 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

Changes to the agreed paediatric investigation plan for palovarotene, capsule, hard, 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

A waiver for palovarotene, capsule, hard, oral use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby refused.

Article 3

This decision is addressed to Ipsen Pharma, 65 quai George Gorse, 92100 - Boulogne-Billancourt, France.

EMA/PDCO/483825/2021 Corr
Amsterdam, 12 November 2021

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

EMEA-001662-PIP01-14-M05

Scope of the application

Active substance(s):

Palovarotene

Condition(s):

Treatment of fibrodysplasia ossificans progressiva

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Ipsen Pharma

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Ipsen Pharma submitted to the European Medicines Agency on 6 August 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0127/2015 issued on 5 June 2015, the decision P/0364/2017 issued on 1 December 2017, the decision P/0121/2018 issued on 11 April 2018, the decision P/0144/2020 issued on 15 April 2020 and the decision P/0441/2020 issued on 1 December 2020.

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

The procedure started on 14 September 2021.

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.
   - to refuse the granting of a waiver for some of the subsets of the paediatric population and the above mentioned condition(s) as it does not meet the grounds detailed in Article 11(1) 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 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.

1.1. Condition:

Treatment of fibrodysplasia ossificans progressiva

The request for the waiver applied to:

- females less than 9 years of age and males less than 11 years of age;
- capsule, hard, oral use.

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 fibrodysplasia ossificans progressiva

2.1.1. Indication(s) targeted by the PIP

Treatment of fibrodysplasia ossificans progressiva

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)

Capsule, hard

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	2	**Study 1** Dose range-finding juvenile toxicity study (9000317) **Study 2** Juvenile toxicity study (6700132)
Clinical studies	4	**Study 3** Multicentre, randomised, double-blind, placebo-controlled dose-finding, proof-of-concept study to evaluate the ability of different doses of palovarotene to prevent heterotopic ossification (HO) at the flare-up site in subjects with fibrodysplasia ossificans progressiva (FOP) (PVO-1A-201) **Study 4** Multicentre, open-label study to evaluate the safety and activity of different palovarotene dosing regimens in subjects with FOP in four parts (Part A, B, C and D) (PVO-1A-202) **Study 5** Multicentre, open label study to evaluate the efficacy of palovarotene in decreasing heterotopic ossification (HO) as compared to untreated subjects from study 6 and to evaluate the safety of palovarotene in subjects with FOP (PVO-1A-301) **Study 6** Longitudinal, non-interventional two-part (A and B) study to determine the natural course of the disease for 36 months in subjects with FOP (PVO-1A-001)
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 June 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes