MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan

MHRA-100296-PIP01-21-M01

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 Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Ipsen Limited submitted to the licensing authority on 04/10/2021 16:54 BST an application for a Modification

The procedure started on 29/07/2022 15:29 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100296-PIP01-21-M01

Of 19/10/2022 16:46 BST

On the adopted decision for palovarotene (MHRA-100296-PIP01-21-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan

This decision applies to a Modification for palovarotene, Capsule, hard , Oral use .

This decision is addressed to Ipsen Limited, 190 Bath Road, Slough, Berkshire, SL1 3XE, UK, Slough, United Kingdom, SL1 3XE

ANNEX I

1. Waiver

1.1 Condition:

Treatment of fibrodysplasia ossificans progressiva Reason for granting waiver: Not Applicable The request for a waiver applied to: Paediatric Subset(s): Females less than 9 years of age and males less than 11 years of age; Pharmaceutical form(s): Capsule, hard Route(s) of administration: Oral use Reason for Refusing Waiver: • the MHRA 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 MHRA

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of fibrodysplasia ossificans progressiva

2.2 Indication(s) targeted by the PIP:

Treatment of fibrodysplasia ossificans progressiva

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	2	Study 1(9000317) Dose range-finding juvenile toxicity study Study 2 (6700132) Juvenile toxicity study
Clinical Studies	4	Study 3 (PVO-1A-201) 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) Study 4 (PVO-1A-202) 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). Study 5 (PVO-1A-301) 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. Study 6 (PVO-1A-001) Longitudinal, non-interventional two-part (A and B) study to determine the natural course of the disease for 36 months in subjects with FOP.
Extrapolation, Modeling & Simulation Studies	0	Not applicable

Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/06/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes