EMA/182557/2019

European Medicines Agency decision

P/0123/2019

of 17 April 2019

on the acceptance of a modification of an agreed paediatric investigation plan for selexipag (Uptravi), (EMEA-000997-PIP01-10-M02) 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/246/2011 issued on 21 October 2011 and the decision P/0154/2013 issued on 5 July 2013,

Having regard to the application submitted by Janssen Cilag International NV on 14 November 2018 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 1 March 2019, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 to the deferral and to the waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral and to the 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 selexipag (Uptravi), film-coated tablet, tablet, oral use, including changes to the deferral and to the waiver, 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

This decision is addressed to Janssen Cilag International NV, Turnhoutseweg 30, B-2340 – Beerse, Belgium.

EMA/PDCO/842340/2018
London, 1 March 2019

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

EMEA-000997-PIP01-10-M02

Scope of the application

Active substance(s):

Selexipag

Invented name:

Uptravi

Condition(s):

Treatment of pulmonary arterial hypertension

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Janssen Cilag International NV

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen Cilag International NV submitted to the European Medicines Agency on 14 November 2018 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/246/2011 issued on 21 October 2011 and the decision P/0154/2013 issued on 5 July 2013.

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

The procedure started on 3 January 2019.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan and the waiver 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 and to the deferral and to the waiver in the scope set out in the Annex I of this opinion.

   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 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 annexes 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 pulmonary arterial hypertension

The waiver applies to:

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

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of pulmonary arterial hypertension

2.1.1. Indication(s) targeted by the PIP

Treatment of pulmonary arterial hypertension (PAH)

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)

Film-coated tablet

Tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of mini tablets (diameter ≤ 3mm), which can be taken dispersed in water
Non-clinical studies	2	**Study 2** 28 day dose range finding toxicity study in juvenile dogs **Study 3** 39 week toxicity study in juvenile dogs

Clinical studies	2	**Study 4** This study was deleted as a result of procedure EMEA-000997-PIP01-10-M02. **Study 5** This study was deleted as a result of procedure EMEA-000997-PIP01-10-M02. **Study 6** Open-label, single-arm study to evaluate the safety, tolerability and pharmacokinetics of selexipag in children from 2 to less than 18 years of age with pulmonary arterial hypertension (PAH) **Study 7** Double-blind, randomised, placebo-controlled, parallel group, event driven efficacy study with open-label extension period to assess selexipag as add-on to standard of care in children from 2 to less than 18 years with pulmonary arterial hypertension (PAH)
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 December 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

Treatment of pulmonary arterial hypertension

Authorised indication(s):

- Uptravi is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II–III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 (PDE-5) inhibitor, or as monotherapy in patients who are not candidates for these therapies.
- Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use