EMA/469191/2023

# European Medicines Agency decision

P/0417/2023

of 25 October 2023

on the acceptance of a modification of an agreed paediatric investigation plan for selexipag (Uptravi), (EMEA-000997-PIP01-10-M07) 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 Union procedures for the authorisation and supervision of medicinal products for human 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, the decision P/0154/2013 issued on 5 July 2013, the decision P/0123/2019 issued on 17 April 2019, the decision P/0328/2021 issued on 13 August 2021, and the decision P/0088/2023 issued on 10 March 2023,

Having regard to the application submitted by Janssen-Cilag International NV on 30 May 2023 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 8 September 2023, 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.

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

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

***Article 1***

Changes to the agreed paediatric investigation plan for selexipag (Uptravi), film-coated tablet, 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***

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

EMA/PDCO/264812/2023 Corr[1]
Amsterdam, 8 September 2023

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

EMEA-000997-PIP01-10-M07

## Scope of the application

**Active substance(s):**

Selexipag

**Invented name and authorisation status:**

See Annex II

**Condition(s):**

Treatment of pulmonary arterial hypertension

**Pharmaceutical form(s):**

Film-coated tablet

**Route(s) of administration:**

Oral use

**Name/corporate name of the PIP applicant:**

Janssen-Cilag International NV

## 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 30 May 2023 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, the decision P/0154/2013 issued on 5 July 2013, the decision P/0123/2019 issued on 17 April 2019, the decision P/0328/2021 issued on 13 August 2021, and the decision P/0088/2023 issued on 10 March 2023.

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

The procedure started on 10 July 2023.

[1] Corr 20 October 2023

## Scope of the modification

Some measures 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 in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway 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, 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 years to less than 18 years of age

### 2.1.3. Pharmaceutical form(s)

Film-coated tablet

### 2.1.4. Measures

| **Area** | **Description** |
|---|---|
| Quality-related studies | **Study 1**<br>Development of mini tablets (diameter ≤ 3mm). |
| Non-clinical studies | **Study 2**<br>28-day dose range finding toxicity study in juvenile dogs.<br>**Study 3**<br>39-week toxicity study in juvenile dogs |
| Clinical studies | **Study 4**<br>*This study was deleted as a result of procedure EMEA-000997-PIP01-10-M02.* |

| | |
|---|---|
| | **Study 5**<br><br>*This study was deleted as a result of procedure EMEA-000997-PIP01-10-M02.*<br><br>**Study 6**<br><br>Open-label, single-arm study to evaluate the safety, tolerability and pharmacokinetics of selexipag in children from 2 years to less than 18 years of age with pulmonary arterial hypertension (PAH). (AC-065A203)<br><br>**Study 7**<br><br>Double-blind, randomised, placebo-controlled, parallel group study with open-label extension period to assess the efficacy and safety of selexipag as add-on to standard of care in children from 2 years to less than 18 years of age with pulmonary arterial hypertension (PAH). (AC-065A310) |
| Extrapolation, modelling and simulation studies | Not applicable. |
| Other studies | **Study 8**<br><br>*This study was added as a result of procedure EMEA-000997-PIP01-10-M06.*<br><br>Pharmacodynamic (PD) similarity/comparison study to compare the PD and clinical responses for efficacy based on Study 6 (AC-065A203), Study 7 (AC-065A310) and Study AC-065A302 in paediatric participants from 2 years to less than 18 years of age and adult participants with PAH. |
| Other measures | 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

## *Information provided by the applicant:*

## Condition(s) and authorised indication(s)

1. 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.
  - Invented name(s): Uptravi
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure