EMA/616445/2021

European Medicines Agency decision

P/0480/2021

of 3 December 2021

on the acceptance of a modification of an agreed paediatric investigation plan for macitentan (Opsumit), (EMEA-001032-PIP01-10-M04) 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/303/2011 issued on 21 December 2011, the decision P/0087/2012 issued on 25 May 2012 and the decision P/0049/2016 issued on 18 March 2016,

Having regard to the application submitted by Janssen-Cilag International NV on 12 July 2021 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 15 October 2021, 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.

(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.

[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 macitentan (Opsumit), dispersible tablet, film-coated tablet, oral use, including changes to the deferral, 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, BE-2340 – Beerse, Belgium.

EMA/PDCO/403257/2021
Amsterdam, 15 October 2021

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

EMEA-001032-PIP01-10-M04

Scope of the application

Active substance(s):

Macitentan

Invented name:

Opsumit

Condition(s):

Treatment of pulmonary arterial hypertension

Treatment of systemic sclerosis

Treatment of idiopathic pulmonary fibrosis

Authorised indication(s):

Treatment of pulmonary arterial hypertension

Pharmaceutical form(s):

Dispersible tablet

Film-coated 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

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 12 July 2021 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/303/2011 issued on 21 December 2011, the decision P/0087/2012 issued on 25 May 2012 and the decision P/0049/2016 issued on 18 March 2016.

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

The procedure started on 17 August 2021.

A meeting with the Paediatric Committee took place on 13 October 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 and to the deferral 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 systemic sclerosis

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- dispersible tablet, film-coated tablet, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

1.2. Condition:

Treatment of idiopathic pulmonary fibrosis

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- dispersible tablet, film-coated tablet, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended occurs only in adult populations.

1.3. Condition:

Treatment of pulmonary arterial hypertension

The waiver applies to:

- All subsets of the paediatric population from birth to less than 1 month of age;
- dispersible tablet, film-coated tablet, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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 1 month to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Dispersible tablet

Film-coated tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1:** Development of a dispersible tablet formulation. **Study 2:** *This study was deleted during procedure EMEA-001032-PIP01-10-M02.*
Non-clinical studies	2	**Study 3:** 25-day dose range finding toxicity study in juvenile rats. **Study 4:** Toxicity study in juvenile rats.
Clinical studies	1	**Study 5:** *This study was deleted during procedure EMEA-001032-PIP01-10-M02.* **Study 6:** *This study was deleted during procedure EMEA-001032-PIP01-10-M02.* **Study 7:** *This study was deleted during procedure EMEA-001032-PIP01-10-M02.* **Study 8:** Open-label, randomised, multicentre, active controlled, parallel group study to evaluate pharmacokinetics, safety and efficacy of macitentan in children from 1 month to less than 18 years of age with pulmonary arterial hypertension.
Extrapolation, modelling and simulation studies	2	**Study 9:** *(This study was added as a result of procedure EMEA-001032-PIP01-10-MO4.)* Population pharmacokinetic modelling and simulation study to support extrapolation and the use of macitentan in children from 1 month to less than 18 years of age with pulmonary arterial hypertension

		Study 10: *(This study was added as a result of procedure EMEA-001032-PIP01-10-MO4.)* Pharmacodynamic similarity/comparison study
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 March 2023
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of pulmonary arterial hypertension

Authorised indication(s):

- As monotherapy or in combination for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use