EMA/315432/2021

European Medicines Agency decision

P/0242/2021

of 7 July 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for macitentan (Opsumit), (EMEA-001032-PIP03-19) 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 application submitted by Janssen-Cilag International N.V. on 20 December 2019 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 May 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation 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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting 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

A paediatric investigation plan for macitentan (Opsumit), film-coated tablet, dispersible tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for macitentan (Opsumit), film-coated tablet, dispersible tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for macitentan (Opsumit), film-coated tablet, dispersible tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/303/2011 issued on 21 December 2011, including subsequent modifications thereof.

Article 5

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

EMA/PDCO/120151/2021
Amsterdam, 21 May 2021

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001032-PIP03-19

Scope of the application

Active substance(s):

Macitentan

Invented name:

Opsumit

Condition(s):

Treatment of functional single ventricle heart disease with total cavo-pulmonary connection

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Dispersible tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Janssen-Cilag International N.V.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International N.V. submitted for agreement to the European Medicines Agency on 20 December 2019 an application

for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 28 January 2020.

Supplementary information was provided by the applicant on 11 February 2021. The applicant proposed modifications to the paediatric investigation plan and requested a deferral.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 functional single ventricle heart disease with total cavo-pulmonary connection

The waiver applies to:

- the paediatric population without total cavo-pulmonary connection;
- all pharmaceutical forms, all routes of administration;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset.

2. Paediatric investigation plan

2.1. Condition:

Treatment of functional single ventricle heart disease with total cavo-pulmonary connection

2.1.1. Indication(s) targeted by the PIP

Treatment of functional single ventricle heart disease in adolescents and children to improve exercise capacity.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

The paediatric population with total cavo-pulmonary connection

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Dispersible tablet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	3	**Study 1 (AC-055H301, RUBATO)** Double-blind, randomised, placebo-controlled trial to evaluate efficacy of macitentan in adolescents from 12 years to less than 18 years of age (and adults) with functional single ventricle heart disease and total cavo-pulmonary connection (TCPC) for the improvement of exercise capacity

		Study 2 (AC-055H302, RUBATO-OL) Open-label, single-arm trial to evaluate safety and tolerability of macitentan in adolescents from 12 years to less than 18 years of age (and adults) with functional single ventricle heart disease and TCPC **Study 3** Open-label single-arm study to assess the pharmacokinetics, pharmacodynamics and safety of macitentan in children and adolescents younger than 18 years of age with functional single ventricle heart disease and TCPC
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 2025
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):

1. Treatment pulmonary arterial hypertension

Authorised indication(s):

- Opsumit, as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III;
- 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 (see section 5.1).

Authorised pharmaceutical form(s):

Film-coated tablets

Authorised route(s) of administration:

Oral use