EMA/672726/2022

European Medicines Agency decision

P/0348/2022

of 10 August 2022

on the acceptance of a modification of an agreed paediatric investigation plan for setmelanotide (Imcivree), (EMEA-002209-PIP01-17-M03) 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.

European Medicines Agency decision

P/0348/2022

of 10 August 2022

on the acceptance of a modification of an agreed paediatric investigation plan for setmelanotide (Imcivree), (EMEA-002209-PIP01-17-M03) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0164/2018 issued on 15 June 2018, decision P/0179/2020 issued on 15 May 2020, and decision P/0215/2021 issued on 8 June 2021,

Having regard to the application submitted by Rhythm Pharmaceuticals, Inc on 17 March 2022 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 24 June 2022, 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 setmelanotide (Imcivree), solution for injection, subcutaneous 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 Rhythm Pharmaceuticals, Inc, 222 Berkeley Street, 12th Floor, MA 02116 - Boston, USA.

EMA/PDCO/178323/2022
Amsterdam, 24 June 2022

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

EMEA-002209-PIP01-17-M03

Scope of the application

Active substance(s):

Setmelanotide

Invented name:

Imcivree

Condition(s):

Treatment of appetite and general nutrition disorders

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Rhythm Pharmaceuticals, Inc

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Rhythm Pharmaceuticals, Inc submitted to the European Medicines Agency on 17 March 2022 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/0164/2018 issued on 15 June 2018, decision P/0179/2020 issued on 15 May 2020, and decision P/0215/2021 issued on 8 June 2021.

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

The procedure started on 25 April 2022.

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 to the paediatric investigation plan 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 appetite and general nutrition disorders

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- solution for injection, subcutaneous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition

Treatment of appetite and general nutrition disorders

2.1.1. Indication(s) targeted by the PIP

Treatment of obesity and/or hyperphagia associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway

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)

Solution for injection

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of a formulation which does not contain DSPE/mPEG and which has a dose interval longer than 1 day (ideally 1 week). **Study 2** Development of a device capable of accurate and reproducible delivery of the lowest dosing volume required.
Non-clinical studies	**Study 3** Evaluation of mPEG-DSPE in rat and monkey brain from chronic toxicity studies by immunohistochemistry. The objective is to determine localization of mPEG-DSPE in rat and monkey brain. (RM-493-TOX-023 and RM-493-TOX-024)

	Study 4 Evaluation of the absorption, distribution, metabolism and elimination of mPEG-DSPE in rat using 14C-mPEG-DSPE (labelled on mPEG only).
Clinical studies	**Study 5** Open-label, 1-year study to evaluate the pharmacokinetics, safety and efficacy of setmelanotide in children from 6 to less than 18 years of age (and in adults) with Proopiomelanocortin (POMC) deficiency obesity. (Study RM-493-012) **Study 6** Open-label, uncontrolled, 3-months study, to evaluate the pharmacokinetics, safety and efficacy of setmelanotide in children from 6 to less than 18 years of age (and in adults) with rare genetic disorders of obesity. (RM-493-014) **Study 7** Open-label, 1-year study to evaluate the pharmacokinetics, safety and efficacy of setmelanotide in children from 6 to less than 18 years of age (and in adults) with leptin receptor (LEPR) deficiency obesity. (Study RM-493-015) **Study 8** *Study added during modification EMEA-002209-PIP01-17-M02.* Open-label, non-comparative study to assess the safety and activity of setmelanotide in obese children with Proopiomelanocortin (POMC) deficiency, prohormone convertase 1 (PCSK1) deficiency or leptin receptor (LEPR) deficiency and Bardet-Biedl syndrome, from 2 years to less than 6 years of age. (RM-493-033)
Extrapolation, modelling and simulation studies	Not applicable.
Other studies	Not applicable.
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:	Yes
Date of completion of the paediatric investigation plan:	By December 2024
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 of obesity and the control of hunger associated with genetic deficiencies of the melanocortin 4 receptor (MC4R) pathway.

Authorised indication(s):

- Treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic pro-opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 6 years of age and above.

Authorised pharmaceutical form(s):

Solution for injection

Authorised route(s) of administration:

Subcutaneous use