EMADOC-1700519818-2096775

European Medicines Agency decision

EMA/PE/0000245434

of 6 May 2025

on the acceptance of a modification of an agreed paediatric investigation plan for setmelanotide (Imcivree) 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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on the acceptance of a modification of an agreed paediatric investigation plan for setmelanotide (Imcivree) 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, the decision P/0179/2020 issued on 15 May 2020, the decision P/0215/2021 issued on 8 June 2021, the decision P/0348/2022 issued on 10 August 2022 and the decision EMA/PE/0000182239 issued on 19 December 2024,

Having regard to the application submitted by Rhythm Pharmaceuticals Inc. on 17 January 2025 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 25 April 2025, 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, 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), 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 Rhythm Pharmaceuticals Inc., 500 Boylston Street Floor 11, 02116-3740 - Boston, United States.

EMADOC-1700519818-1906254

Amsterdam, 25 April 2025

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

EMA/PE/0000245434

Scope of the application

Active substance(s):

Setmelanotide

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of appetite and general nutrition disorders

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Subcutaneous use

Name/corporate name of the PIP applicant:

Rhythm Pharmaceuticals Inc.

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 January 2025 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, the decision P/0179/2020 issued on 15 May 2020, the decision P/0215/2021 issued on 8 June 2021, the decision P/0348/2022 issued on 10 August 2022 and the decision EMA/PE/0000182239 issued on 19 December 2024.

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

The procedure started on 24 February 2025.

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 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** *Study deleted during modification EMA-PE-0000245434* **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) **Study 9** *Study added during modification EMA-PE-0000245434.* Randomised, double-blind, placebo-controlled study to assess the efficacy and safety of setmelanotide in patients with heterozygous gene variant in the POMC gene or PCSK1 gene, heterozygous gene variant in the LEPR gene, homozygous, heterozygous, or compound heterozygous variant in the NCOA1 (SRC1) gene, or homozygous, heterozygous, or compound heterozygous variant in the SH2B1 gene, or chromosomal 16p11.2 deletion encompassing the SH2B1 gene in children from 6 years of age to less than 18 years of age (and in adults). (RM-493-035) **Study 10** *Study added during modification EMA-PE-0000245434.* Open-label study to assess the safety and activity of setmelanotide in obese children with heterozygous gene variant in the POMC gene or PCSK1 gene, heterozygous gene variant in the LEPR gene, homozygous, heterozygous, or compound heterozygous variant in the NCOA1 (SRC1) gene, or homozygous, heterozygous, or compound heterozygous variant in the SH2B1 gene, or chromosomal 16p11.2 deletion encompassing the SH2B1 gene from 2 years to less than 6 years of age.

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 2030
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 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.
  - Invented name(s): Imcivree
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Subcutaneous use
  - Authorised via centralised procedure