EMA/790574/2022

European Medicines Agency decision

P/0462/2022

of 28 October 2022

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for resmetirom (EMEA-003087-PIP01-21) 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/0462/2022

of 28 October 2022

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for resmetirom (EMEA-003087-PIP01-21) 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 application submitted by Madrigal Pharmaceuticals EU Limited on 6 August 2021 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 9 September 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for resmetirom, tablet, age-appropriate oral solid dosage form, 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 resmetirom, tablet, age-appropriate oral solid dosage form, 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 resmetirom, tablet, age-appropriate oral solid dosage form, 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 is addressed to Madrigal Pharmaceuticals EU Limited, 1 Castlewood Avenue, Dublin 6 – Dublin, Ireland.

EMA/PDCO/578867/2022
Amsterdam, 9 September 2022

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

EMEA-003087-PIP01-21

Scope of the application

Active substance(s):

Resmetirom

Condition(s):

Treatment of non-alcoholic steatohepatitis

Pharmaceutical form(s):

Tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Madrigal Pharmaceuticals EU Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Madrigal Pharmaceuticals EU Limited submitted for agreement to the European Medicines Agency on 6 August 2021 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 14 September 2021.

Supplementary information was provided by the applicant on 30 May 2022. The applicant proposed modifications to the paediatric investigation plan.

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)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Paediatric Committee member of Norway 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 annex 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 non-alcoholic steatohepatitis

The waiver applies to:

- the paediatric population from birth to less than 8 years of age;
- tablet, age-appropriate oral solid dosage form, oral 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 non-alcoholic steatohepatitis

2.1.1. Indication(s) targeted by the PIP

Treatment of non-alcoholic steatohepatitis (NASH)

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

From 8 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate oral solid dosage form.
Non-clinical studies	**Study 2 (3196-21-003)** Definitive juvenile toxicity study in rats.
Clinical studies	**Study 3** Open label pharmacokinetic (PK)/pharmacodynamic (PD) single and multiple ascending dose study designed to assess the safety profile and tolerability of resmetirom after single and multiple oral dosing as well as the relationship between dose and/or plasma concentrations of resmetirom and safety biomarkers including the thyroid axis hormones

	and PD parameters (lipids, sex hormone binding globulin (SHBG)) in adolescents from 12 years to less than 18 years of age with NASH. **Study 4** Double-blind, placebo-controlled study to evaluate safety, tolerability, effects on relevant imaging and blood biomarkers and efficacy in post-puberty paediatric patients from 12 years to less than 18 years of age with biopsy-confirmed NASH. **Study 5** Open label pharmacokinetic (PK)/pharmacodynamic (PD) single and multiple ascending dose study designed to assess the safety profile and tolerability of resmetirom after single and multiple oral dosing as well as the relationship between dose and/or plasma concentrations of resmetirom and safety biomarkers including the thyroid axis hormones and PD parameters (lipids, sex hormone binding globulin (SHBG)) in children from 8 years to less than 12 years of age with NASH. **Study 6** Double-blind, placebo-controlled study to evaluate safety, tolerability, effects on relevant imaging and blood biomarkers and efficacy in pre-pubertal paediatric patients from 8 years to less than 12 years of age with biopsy-confirmed NASH.
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:	No
Date of completion of the paediatric investigation plan:	By December 2031
Deferral for one or more measures contained in the paediatric investigation plan:	Yes