MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-102031-PIP01-25

Scope of the Application

Active Substance(s)

resmetirom

Condition(s)

Treatment of metabolic dysfunction-associated steatohepatitis

Pharmaceutical Form(s)

Film coated tablet Age appropriate oral dosage form

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Madrigal Pharmaceuticals EU Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Madrigal Pharmaceuticals EU Limited submitted to the licensing authority on 22/08/2025 21:25 BST an application for a Paediatric Investigation Plan

The procedure started on 27/08/2025 14:01 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to agree a paediatric investigation plan and grant a deferral and grant a waiver

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-102031-PIP01-25

Of 21/11/2025 09:01 GMT

On the adopted decision for resmetirom (MHRA-102031-PIP01-25) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for resmetirom, Film coated tablet Age appropriate oral dosage form , ORAL USE .

This decision is addressed to Madrigal Pharmaceuticals EU Limited , 1 Castlewood Avenue, Dublin, IRELAND, D06 H685

ANNEX I

1. Waiver

1.1 Condition:

Treatment of metabolic dysfunction-associated steatohepatitis The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 years of age Pharmaceutical form(s): Film coated tablet Age-appropriate oral solid dosage form Route(s) of administration: ORAL USE Reason for granting waiver: 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(s):

Treatment of metabolic dysfunction-associated steatohepatitis

2.2 Indication(s) targeted by the PIP:

Treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH)

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 6 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Film-coated tablet Age-appropriate oral solid dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 (AC-SP-01910) Development of an age-appropriate oral solid dosage form.
Non-Clinical Studies	1	Study 2 (3196-21-003) Definitive juvenile toxicity study in rats.
Clinical Studies	3	Study 3 (MGL-3196-29) Open-label, multiple ascending dose study to evaluate safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of resmetirom, as well as the relationship between dose and/or plasma concentrations of resmetirom and PD biomarkers in children from 6 years to less than 18 years of age with metabolic dysfunction-associated steatohepatitis (MASH). Study 4 (MGL-3196-26) Double-blind, randomised, placebo-controlled study to evaluate safety and efficacy of resmetirom in adolescents from 12 years to less than 18 years of age with biopsy confirmed MASH. Study 5 (MGL-3196-XX) Double-blind, randomised, placebo-controlled study to evaluate safety and efficacy of resmetirom in adolescents from 6 years to less than 12 years of age with biopsy confirmed MASH.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
Other Studies	0	Not applicable.

Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	30/11/2037
Deferral of one or more studies contained in the paediatric investigation plan:	Yes