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

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100211-PIP01-21-M01

Scope of the Application

Active Substance(s)

VOLANESORSEN SODIUM

Condition(s)

Treatment of familial chylomicronemia syndrome

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

Subcutaneous use

Name / Corporate name of the PIP applicant

Akcea Therapeutics Ireland Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Akcea Therapeutics Ireland Limited submitted to the licensing authority on 05/10/2021 00:01 BST an application for a Modification

The procedure started on 29/07/2022 14:43 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 accept change(s) to the agreed paediatric investigation plan and to the deferral

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-100211-PIP01-21-M01

Of 13/10/2022 16:15 BST

On the adopted decision for VOLANESORSEN SODIUM (MHRA-100211-PIP01-21-M01) 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 modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for VOLANESORSEN SODIUM, Solution for injection , Subcutaneous use .

This decision is addressed to Akcea Therapeutics Ireland Limited, Regus House, Harcourt Centre, Harcourt Road, Dublin, Ireland, D02 KD58

ANNEX I

1. Waiver

1.1 Condition:

Treatment of familial chylomicronemia syndrome The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Solution for injection Route(s) of administration: Subcutaneous use Reason for granting waiver: on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of familial chylomicronaemia syndrome

2.2 Indication(s) targeted by the PIP:

Treatment of familial chylomicronaemia syndrome

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

The paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Solution for injection

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	0	Not applicable
Clinical Studies	1	Study 1 (ISIS 304801-CS20) Open-label trial to evaluate pharmacokinetics (PK), pharmacodynamics (PD) and safety of volanesorsen in children from 2 years to less than 18 years of age with familial chylomicronaemia syndrome (FCS).
Extrapolation, Modeling & Simulation Studies	3	Study 2 (304801-PPK02) Modelling and simulation study to develop a population PK/PD model, using data from adults, to determine the appropriate dose for children from 12 years to less than 18 years of age with FCS. Study 3 (304801-PPK03) Modelling and simulation study to develop a population PK/PD model, using also data from adolescents in study 1, to determine the appropriate dose for children from 2 years to less than 12 years of age with FCS. Study 4 Extrapolation study to evaluate the similarity of PK, PD and exposure-triglycerides (TG) response relationship of volanesorsen in children from 2 years to less than 18 years of age with FCS compared with adult FCS patients.
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:	Yes
Date of completion of the paediatric investigation plan:	31/01/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes