MHRA
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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-101417-PIP01-24-M01

Scope of the Application

Active Substance(s)

Plozasiran (USAN) (synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues)

Condition(s)

Treatment of hypertriglyceridaemia

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Arrowhead Pharmaceuticals Inc

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Arrowhead Pharmaceuticals Inc submitted to the licensing authority on 06/08/2025 15:21 BST an application for a Modification

The procedure started on 16/09/2025 20:06 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-101417-PIP01-24-M01

Of 23/10/2025 11:02 BST

On the adopted decision for Plozasiran (USAN) (synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues) (MHRA-101417-PIP01-24-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 Plozasiran (USAN) (synthetic double-stranded siRNA oligonucleotide directed against apolipoprotein C-III mRNA and covalently linked to a ligand containing three N-acetylgalactosamine residues), Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Arrowhead Pharmaceuticals Inc, 177 East Colorado Boulevard, Suite 700, Pasadena, UNITED STATES OF AMERICA, CA 91105

ANNEX I

1. Waiver

1.1 Condition:

Treatment of hypertriglyceridaemia 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 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 hypertriglyceridaemia

2.2 Indication(s) targeted by the PIP:

Treatment of Familial chylomicronaemia syndrome (FCS)

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	1	Study 1 Development of a solution for injection for subcutaneous use in appropriate doses for children from 2 years of age to less than 12 years of age.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 2 Open label study to evaluate the activity, pharmacokinetics, pharmacodynamics and safety of plozasiran in adolescents from 12 years to less than 18 years of age with familial chylomicronaemia syndrome (FCS) Study 3 Open label study to evaluate the activity, pharmacokinetics, pharmacodynamics and safety of plozasiran in children from 2 years to less than 12 years of age with familial chylomicronaemia syndrome (FCS)
Extrapolation, Modeling & Simulation Studies	2	Study 4 Modelling and simulation study to develop a population PK/PD model from adults, to determine the appropriate does in adolescents from 12 years of age to less than 18 years of age with FCS Study 5 Modelling and simulation study to develop a population PK/PD model from

		adults, to determine the appropriate does in children from 2 years of age to less than 12 years of age with FCS. Extrapolation Plan Studies 2, 3, 4 and 5 are part of the extrapolation plan of PK and PDA data from adult patients to the paediatric population from 2 years of age to less than 18 years of age with FCS.
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:	29/02/2036
Deferral of one or more studies contained in the paediatric investigation plan:	Yes