MHRA
10 South Colonnade
Canary Wharf
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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-101417-PIP01-24

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)

Familial chylomicronaemia syndrome (FCS)

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 23/04/2024 09:16 BST an application for a Paediatric Investigation Plan

The procedure started on 13/01/2025 11:40 GMT

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-101417-PIP01-24

Of 03/03/2025 09:57 GMT

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) 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 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 familial chylomicronaemia syndrome (FCS)

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of familial chylomicronaemia syndrome (FCS)

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

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 adolescent 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 adolescent 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 dose 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 dose in children from 2 years of age to less than 12 years of age with FCS
Other Studies	0	Not applicable

Other Measures	1	Extrapolation plan: Studies 2, 3, 4 and 5 are part of the extrapolation plan of PK and PD data from adult patients to paediatric population form 2 years of age to less than 18 years of age with FCS.

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