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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

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

MHRA-100789-PIP01-22

Scope of the Application

Active Substance(s)

Fazirsiran

Condition(s)

Treatment of congenital alpha-1 antitrypsin deficiency

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Takeda UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Takeda UK Limited submitted to the licensing authority on 13/01/2023 15:32 GMT an application for a Paediatric Investigation Plan

The procedure started on 30/01/2024 08:22 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-100789-PIP01-22

Of 13/02/2024 17:32 GMT

On the adopted decision for Fazirsiran (MHRA-100789-PIP01-22) 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 Fazirsiran, Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Takeda UK Limited, 1 Kingdom Street, London, UNITED KINGDOM, W2 6BD

ANNEX I

1. Waiver

1.1 Condition:

Treatment of congenital alpha-1 antitrypsin deficiency The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 9 months of age Pharmaceutical form(s): Solution for injection Route(s) of administration: SUBCUTANEOUS 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 congenital alpha-1 antitrypsin deficiency

2.2 Indication(s) targeted by the PIP:

Treatment of alpha-1 antitrypsin deficiency associated liver disease (AATD-LD)

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

The paediatric population from 9 months 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 an age appropriate solution for injection for paediatric patients weighing less than 25 kg.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	1	Study 2 (TAK-999-aaaa) Open-label, multicentre study to evaluate the safety, tolerability, activity and pharmacokinetics (PK) / pharmacodynamics (PD) of fazirsiran in the paediatric population aged 9 months to less than 18 years with AATD-LD with evidence of fibrosis or compensated cirrhosis.
Extrapolation, Modeling & Simulation Studies	2	Study 3 Population pharmacokinetic (PK) and pharmacodynamic (PD) modelling and simulation study to assist with dose-finding and sample size reassessment in the paediatric population aged 9 months to less than 18 years with AATD-LD with evidence of fibrosis or compensated cirrhosis. Extrapolation plan Studies 2 and 3, are part of the extrapolation plan of efficacy data from adult patients to the paediatric population from 9 months to less than 18 years of age with condition AATD-LD.
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:	30/09/2033
Deferral of one or more studies contained in the paediatric investigation plan:	Yes