MHRA
10 South Colonnade
Canary Wharf
London
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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-100424-PIP01-22

Scope of the Application

Active Substance(s)

zilebesiran sodium

Condition(s)

Treatment of Hypertension

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Alnylam Netherlands B.V

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Alnylam Netherlands B.V submitted to the licensing authority on 18/03/2022 19:01 GMT an application for a Paediatric Investigation Plan

The procedure started on 04/07/2022 12:16 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-100424-PIP01-22

Of 24/05/2023 15:39 BST

On the adopted decision for zilebesiran sodium (MHRA-100424-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 zilebesiran sodium, Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Alnylam Netherlands B.V, Antonio Vivaldistraat 150 , Amsterdam, NETHERLANDS, 1083HP

ANNEX I

1. Waiver

1.1 Condition:

Treatment of hypertension 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 the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of hypertension

2.2 Indication(s) targeted by the PIP:

Treatment of hypertension

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	1	Study 1 Definitive juvenile toxicity study in rats.
Clinical Studies	2	Study 2 Double blind, randomised, multidose trial to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety, and efficacy of zilebesiran as monotherapy and as add-on therapy, in children and adolescents from 6 years to less than 18 years of age with hypertension. Study 3 Open label, randomised multidose trial to evaluate the pharmacokinetics (PK), pharmacodynamics (PD), safety and efficacy of zilebesiran, as monotherapy and as add-on therapy, in children from 2 years to less than 6 years of age with hypertension.
Extrapolation, Modeling & Simulation Studies	1	Study 4 Modelling and simulation study, to support the dose selection of zilebesiran in children from 2 years to less than 18 years of age with hypertension.
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:	30/04/2034

Deferral of one or more studies contained in the paediatric investigation plan:	Yes