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 (MHRA-101454-PIP01-24) and to the deferral

MHRA-101454-PIP01-24-M01

Scope of the Application

Active Substance(s)

Donidalorsen

Condition(s)

Treatment of hereditary angioedema

Pharmaceutical Form(s)

Solution for injection

Route(s) of Administration

SUBCUTANEOUS USE

Name / Corporate name of the PIP applicant

Otsuka Pharmaceutical Netherlands B.V.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Otsuka Pharmaceutical Netherlands B.V. submitted to the licensing authority on 22/04/2025 23:53 BST an application for a Modification

The procedure started on 10/06/2025 09:05 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-101454-PIP01-24-M01

Of 08/08/2025 15:18 BST

On the adopted decision for Donidalorsen (MHRA-101454-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 Donidalorsen, Solution for injection , SUBCUTANEOUS USE .

This decision is addressed to Otsuka Pharmaceutical Netherlands B.V., Herikerbergweg 292,, Amsterdam, NETHERLANDS, CT 1101

ANNEX I

1. Waiver

1.1 Condition:

Treatment of hereditary angioedema 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 does not represent a significant therapeutic benefit as clinical studies are not feasible.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of hereditary angioedema

2.2 Indication(s) targeted by the PIP:

Routine prevention of recurrent attacks of hereditary angioedema in patients aged 2 years and older

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 mice.
Clinical Studies	3	Study 2 (ISIS 721744-CS5) Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of donidalorsen in adolescents from 12 years to less than 18 years of age (and adults) with hereditary angioedema (HAE). Study 3 (ISIS 721744-CS7) Open-label, follow-up trial to evaluate long-term safety and efficacy of donidalorsen in adolescents from 12 years to less than 18 years of age (and adults) with hereditary angioedema (HAE). Study 4 (ISIS 721744-CS8) Open-label, uncontrolled trial to evaluate safety, activity and pharmacokinetics (PK) of donidalorsen in children from 2 years to less than 12 years of age with hereditary angioedema (HAE).
Extrapolation, Modeling & Simulation Studies	1	Study 5 Modelling and simulation study to evaluate the use of donidalorsen in children from 2 years to less than 12 years of age with hereditary angioedema (HAE).
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:	31/12/2029
Deferral of one or more studies contained in the paediatric investigation plan:	Yes