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-101047-PIP01-23

Scope of the Application

Active Substance(s)

vesleteplirsen

Condition(s)

Treatment of Duchenne muscular dystrophy

Pharmaceutical Form(s)

Powder for concentrate for solution for infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Sarepta International UK LTD.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Sarepta International UK LTD. submitted to the licensing authority on 23/08/2023 00:04 BST an application for a Paediatric Investigation Plan

The procedure started on 26/01/2024 07:25 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-101047-PIP01-23

Of 24/09/2024 07:18 BST

On the adopted decision for vesleteplirsen (MHRA-101047-PIP01-23) 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 vesleteplirsen , Powder for concentrate for solution for infusion , INTRAVENOUS USE .

This decision is addressed to Sarepta International UK LTD., Hill House, 1 Little New Street, London, UNITED KINGDOM, EC4A3TR

ANNEX I

1. Waiver

1.1 Condition:

Treatment of Duchenne muscular dystrophy (DMD) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age Pharmaceutical form(s): Powder for concentrate for solution for infusion Route(s) of administration: INTRAVENOUS 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 Duchenne muscular dystrophy (DMD)

2.2 Indication(s) targeted by the PIP:

Treatment of Duchenne muscular dystrophy (DMD)

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Powder for concentrate for solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	2	Study 1 (SR-20-028) Definitive juvenile toxicity study of vesleterplirsen in rats with a 1-month recovery period. Study 2 (SR-17-092) Definitive juvenile toxicity study of vesleterplirsen in rats with a 2-months recovery period.
Clinical Studies	5	Study 3 (5051-102) Open label, pharmacodynamic and pharmacokinetic study of vesleteplirsen in ambulant and non-ambulant paediatric patients from 7 years to less than 18 years of age with DMD with a deletion mutation amenable to exon 51 skipping. Study 4 (5051-201) Two-part open-label, multiple ascending dose, pharmacodynamic and pharmacokinetic study of vesleteplirsen in ambulant and non-ambulant paediatric patients from 7 years to less than 18 years of age (and adults) with DMD with a deletion mutation amenable to exon 51 skipping. Study 5 (5051-301) Two part, double-blind, placebo controlled safety and efficacy study of vesleteplirsen in ambulant paediatric patients from 6 years to less than 15 years of age with DMD with a deletion mutation amenable to exon 51 skipping

		with a treatment and observation period. Study 6 (5051-104) Open-label pharmacokinetic and pharmacodynamic study of vesleteplirsen in ambulant paediatric patients from 6 months to less than 7 years of age with DMD with a deletion mutation amenable to exon 51 skipping. Study 7 (5051-302) Two part, double-blind, placebo controlled safety and efficacy study of vesleteplirsen in non-ambulant paediatric patients less than 18 years of age (and adults) with DMD with a deletion mutation amenable to exon 51 skipping with a treatment and observation period.
Extrapolation, Modeling & Simulation Studies	3	Study 8 Physiologically based pharmacokinetic (PBPK) modelling analysis for mechanistic understanding of vesleteplirsen disposition in the body and to support dose selection for the paediatric population from 6 months to less than 7 years of age. Study 9 Population PK model of vesleteplirsen to characterise vesleteplirsen PK in DMD patients and inform dose selection in paediatric patients of different age groups and support extrapolation in patients below 4 years of age based on similarity of exposure. Extrapolation plan Studies 5,6,8,9 are part of an extrapolation plan covering the paediatric population from 6 months to less than 6 years of age, as agreed by the Regulatory Agency.
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:	Yes
Date of completion of the paediatric investigation plan:	31/03/2032
Deferral of one or more studies contained in the paediatric investigation plan:	Yes