EMA/351272/2023

European Medicines Agency decision

P/0333/2023

of 8 September 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for vesleteplirsen, (EMEA-003305-PIP01-22) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Sarepta Therapeutics Ireland on 8 August 2022 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 July 2023, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for vesleteplirsen, powder for concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for vesleteplirsen, powder for concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for vesleteplirsen, powder for concentrate for solution for infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Sarepta Therapeutics Ireland, Regus House, Harcourt Centre, Harcourt Road, DO2 HW77 - Dublin 2, Ireland.

EMA/PDCO/203853/2023
Amsterdam, 21 July 2023

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-003305-PIP01-22

Scope of the application

Active substance(s):

Vesleteplirsen

Invented name and authorisation status:

See Annex II

Condition(s):

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 Therapeutics Ireland

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Sarepta Therapeutics Ireland submitted for agreement to the European Medicines Agency on 08 August 2022 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 12 September 2022.

Supplementary information was provided by the applicant on 24 April 2023. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of Duchenne muscular dystrophy (DMD)

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- powder for concentrate for solution for infusion, intravenous use;
- 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:

Treatment of Duchenne muscular dystrophy

2.1.1. Indication(s) targeted by the PIP

Treatment of Duchenne muscular dystrophy (DMD)

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 months to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for concentrate for solution for infusion

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** Definitive juvenile toxicity study of vesleterplirsen in rats with a 1-month recovery period (**SR-20-028**). **Study 2** Definitive juvenile toxicity study of vesleterplirsen in rats with a 2-months recovery period (**SR-17-092**).
Clinical studies	**Study 3** 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 (**5051-102**).

	Study 4 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 (**5051-201).** **Study 5** Two part, double-blind, controlled versus placebo 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 (**5051-301)**. **Study 6** 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 (**5051-104**). **Study 7** Two part, double-blind, controlled versus placebo 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 (**5051-302)**.
Modelling and simulation studies	**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 characterize 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.
Other studies	Not applicable.
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 PDCO.

3. Follow-up, completion, and deferral of PIP

Concerns on potential long-term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2032
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

The product is not authorised anywhere in the European Community.