EMA/7958/2022

European Medicines Agency decision

P/0015/2022

of 31 January 2022

on the acceptance of a modification of an agreed paediatric investigation plan for onasemnogene abeparvovec (Zolgensma), (EMEA-002168-PIP01-17-M04) 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 European Medicines Agency's decision P/0272/2018 issued on 14 August 2018, the decision P/0162/2019 issued on 17 April 2019, and decision P/0315/2019 issued on 11 September 2019 and the decision P/0379/2020 issued on 9 September 2020,

Having regard to the application submitted by Novartis Gene Therapy EU Limited on 13 September 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 17 December 2021, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[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

Changes to the agreed paediatric investigation plan for onasemnogene abeparvovec (Zolgensma), solution for injection/infusion, intravenous use, intrathecal use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Novartis Gene Therapy EU Limited, Block B, The Crescent Building, Northwood, Santry, D09 C6X8 - Dublin 9, Ireland.

EMA/PDCO/522825/2021
Amsterdam, 17 December 2021

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-002168-PIP01-17-M04

Scope of the application

Active substance(s):

Onasemnogene abeparvovec

Invented name:

Zolgensma

Condition(s):

Treatment of spinal muscular atrophy

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Solution for injection/infusion

Route(s) of administration:

Intravenous use

Intrathecal use

Name/corporate name of the PIP applicant:

Novartis Gene Therapy EU Limited

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Gene Therapy EU Limited submitted to the European Medicines Agency on 13 September 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0272/2018 issued on 14 August 2018, the decision P/0162/2019 issued on 17 April 2019, and decision P/0315/2019 issued on 11 September 2019 and the decision P/0379/2020 issued on 9 September 2020.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 19 October 2021.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion.

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

2. The measures and timelines of the paediatric investigation plan 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

Not applicable

2. Paediatric investigation plan

2.1. Condition

Treatment of spinal muscular atrophy

2.1.1. Indication(s) targeted by the PIP

Treatment of spinal muscular atrophy

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Solution for injection/infusion

2.1.4. Studies

Area	Number of studies	Description
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	7	**Study 1** Open-label, dose-escalation study to assess the efficacy, safety and tolerability of a single dose of onasemnogene abeparvovec (AVXS-101) administered intravenously in children equal or less than 6 months of age at the time of the dosing with proven mutation of the SMN1 gene. (Study AVXS-101-CL-101) **Study 2** Open-label, dose-comparison, historical controlled study to assess the efficacy, safety and tolerability of a single dose of AVXS-101 administered intrathecally in children equal or older than 6 months and up to 60 months (1800 days) of age at the time of the dosing with a genetic diagnosis consistent with SMA, bi-allelic deletion of SMN1 and 3 copies of SMN2 without the genetic modifier who demonstrate the ability to sit unassisted for 10 or more seconds but cannot stand or walk at the time of study entry. (Study AVXS-101-CL-102)

		Study 3 Open-label, historical controlled study to assess the efficacy, safety and tolerability of a single dose of AVXS-101 administered intravenously in children younger than 6 months of age (180 days) at the time of dosing with Spinal Muscular Atrophy Type 1 with One or Two SMN2 Copies. (Study AVXS-101-CL-302) **Study 4** Open-label, historical controlled study to assess the efficacy, safety and tolerability of a single dose of AVXS-101 administered intravenously in children younger of 6 months of age (180 days) with Spinal Muscular Atrophy Type 1 with One or Two SMN2 Copies. (AVXS-101-CL-303) **Study 5** Open-label, historical controlled study to assess the efficacy, safety and tolerability of a single dose of AVXS-101 administered intravenously to pre-symptomatic patients equal or younger than 6 weeks of age (≤42 days) at time of treatment with SMA with bi-allelic deletion of SMN1 with 2 or 3 copies of SMN2. (AVXS-101-CL-304) **Study 6** *This study was deleted as a result of procedure EMEA-002168-PIP01-17-M04.* **Study 8** *This study was added in procedure EMEA-002168-PIP01-17-M04.* Randomised, double-blind, sham-controlled study to evaluate efficacy, safety, and tolerability of a single dose of onasemnogene abeparvovec administered intrathecally in patients able to sit but have never walked from 2 years to less than 18 years of age with Type 2 SMA with biallelic pathogenic variants of SMN1 and 2-4 copies of SMN2. (OAV101B12301) **Study 9** *This study was added in procedure EMEA-002168-PIP01-17-M04.* Open label, single-arm study to evaluate safety and efficacy of onasemnogene abeparvovec administered intrathecally in patients from 2 years to less than 13 years of age with all types of SMA with bi-allelic SMN1 and any copy of SMN2 and who discontinued treatment with nusinersen and/or risdiplam. (OAV101B12302)
Extrapolation, modelling and simulation studies	0	Not applicable
Other studies	0	Not applicable

Other measures	1	**Measure 7** Disease Registry: A registry should be set up to enroll patients treated with at least AVXS-101 from centers worldwide for a long-term follow-up study (AVXS-101-LT-001) examining the lasting safety and efficacy of AVXS-101 for at least 15 years. (AVXS-101-RG-001)

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 December 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of spinal muscular atrophy

Authorised indication(s):

- Treatment of patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the *SMN1* gene and a clinical diagnosis of SMA Type 1, or patients with 5q SMA with a bi-allelic mutation in the *SMN1* gene and up to 3 copies of the *SMN2* gene.

Authorised pharmaceutical form(s):

Solution for infusion

Authorised route(s) of administration:

Intravenous use