EMA/538802/2018

European Medicines Agency decision

P/0272/2018

of 14 August 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral for onasemnogenum abeparvovecum (EMEA-002168-PIP01-17) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by AveXis Netherlands B.V. on 12 May 2017 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 27 July 2018, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.

(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.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for onasemnogenum abeparvovecum, solution for injection/infusion, intravenous use, intrathecal 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 onasemnogenum abeparvovecum, solution for injection/infusion, intravenous use, intrathecal 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

This decision is addressed to AveXis Netherlands B.V., Gustav Mahlerplein 2, 1082 MA - Amsterdam, The Netherlands.

EMA/PDCO/295054/2018
London, 27 July 2018

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

EMEA-002168-PIP01-17

Scope of the application

Active substance(s):

Onasemnogenum abeparvovecum

Condition(s):

Treatment of spinal muscular atrophy

Pharmaceutical form(s):

Solution for injection/infusion

Route(s) of administration:

Intravenous use

Intrathecal use

Name/corporate name of the PIP applicant:

AveXis Netherlands B.V.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AveXis Netherlands B.V. submitted for agreement to the European Medicines Agency on 12 May 2017 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 20 June 2017.

Supplementary information was provided by the applicant on 7 May 2018. The applicant proposed modifications to the paediatric investigation plan.

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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.

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

2. The measures and timelines of the agreed 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 annex 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	6	**Study 1** Open-label, dose-escalation study to assess the efficacy, safety and tolerability of a single dose of 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)

Area	Number of studies	Description
		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, 3, or 4 copies of SMN2.(AVXS-101-CL-304) **Study 6** Open-label, historical controlled study to assess the efficacy, safety and tolerability of a single dose of AVXS-101 administered intrathecally in patients aged equal or older than6 months to equal or younger than 18 years of age at the time of dosing with spinal muscular atrophy (SMA) Types 1, 2, and 3. (AVXS-101-CL-305)
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 March 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes