EMA/339288/2023

European Medicines Agency decision

P/0291/2023

of 4 August 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver for XEN1101 (EMEA-003271-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 Xenon Pharmaceuticals Inc. on 30 June 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 23 June 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 refusal 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 refusing 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 XEN1101, capsule, hard, age-appropriate oral liquid dosage form, age-appropriate intravenous dosage form, oral use, 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 XEN1101, capsule, hard, age-appropriate oral liquid dosage form, age-appropriate intravenous dosage form, oral use, 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 XEN1101, capsule, hard, age-appropriate oral liquid dosage form, age-appropriate intravenous dosage form, oral use, 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 refused.

Article 4

This decision is addressed to Xenon Pharmaceuticals Inc., 200-3650 Gilmore Way, V5G 4W8 - Burnaby, BC, Canada.

EMA/PDCO/162334/2023
Amsterdam, 23 June 2023

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

EMEA-003271-PIP01-22

Scope of the application

Active substance(s):

XEN1101

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of focal onset seizures

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral liquid dosage form

Age-appropriate intravenous dosage form

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

Xenon Pharmaceuticals Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Xenon Pharmaceuticals Inc. submitted for agreement to the European Medicines Agency on 30 June 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 16 August 2022.

Supplementary information was provided by the applicant on 16 March 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 refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population and the above mentioned condition as it does not meet the grounds detailed in Article 11(1) of said Regulation.

   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

Not applicable

1.1. Condition:

Treatment of focal onset seizures

The request for the waiver applied to:

- the paediatric population from birth to less than one month of age;
- capsule, hard and age-appropriate oral liquid dosage form, age-appropriate intravenous dosage form, intravenous use, oral use;

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

- (a) the specific medicinal product is likely to be ineffective or unsafe in the paediatric population;

Because:

- the PDCO disagreed with the applicant(s)' argumentation that the specific medicinal product is likely to be ineffective or unsafe.

The waiver request is therefore refused by the PDCO.

2. Paediatric investigation plan

2.1. Condition:

Treatment of focal onset seizures

2.1.1. Indication(s) targeted by the PIP

Treatment of focal onset seizures

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)

Capsule, hard

Age-appropriate oral liquid dosage form

Age-appropriate intravenous dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1 (CMC01)**

	Development of an age-appropriate oral reconstitutable liquid dosage form for children from 1 month of age **Study 2 (CMC02)** Development of an age-appropriate intravenous dosage form for neonates from birth to 1 month of age
Non-clinical studies	**Study 3 (NS01)** Dose range-finding juvenile toxicity study to evaluate the use of the product in paediatric population **Study 4 (NS2)** Definitive juvenile toxicity study to evaluate the use of XEN1101 in paediatric population
Clinical studies	**Study 5 (CX01)** Open-label study to evaluate the PK, safety, tolerability and activity of XEN1101 in paediatric patients from 2 years to less than 18 years of age with focal onset seizures (FOS) **Study 6 (CX02)** Open-label study to evaluate the PK, safety, tolerability and activity of XEN1101 in paediatric patients from 1 month less than 2 years of age with focal onset seizures (FOS) **Study 7 (CX03)** Long-term open-label study to evaluate safety, tolerability and activity of XEN1101 in paediatric patients 1 month to less than 18 years of age with focal onset seizures (FOS) **Study 8** Open-label, parallel-group study to evaluate safety, tolerability and efficacy study of adjunctive XEN1101 treatment of neonatal seizures in term neonates
Modelling and simulation studies	**Study 9 (MS01)** Modelling and simulation population PK (popPK), to evaluate the use of XEN1101 in the treatment of focal onset seizures in children from 1 month to less than 18 years of age **Study 10 (MS02)** Modelling and simulation physiologically based PK (PBPK), to evaluate the use of XEN1101 in the treatment of focal onset seizures in infants and children from 1 month to less than 2 years of age and in treatment of neonatal seizures in infants from birth to less than 1 month of age
Other studies	Not applicable

Extrapolation plan	Studies 4, 5 and 6 are part of an extrapolation plan covering the paediatric population from 1 month to less than 18 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:	No
Date of completion of the paediatric investigation plan:	By January 2030
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.