EMA/629449/2022

European Medicines Agency decision

P/0287/2022

of 11 August 2022

on the agreement of a paediatric investigation plan and on the granting of a deferral for doxecitine / doxribtimine (EMEA-003210-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 Zogenix ROI Limited on 17 March 2022 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 24 June 2022, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for doxecitine / doxribtimine, powder for oral solution, oral use, gastric 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 doxecitine / doxribtimine, powder for oral solution, oral use, gastric 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 Zogenix ROI Limited, Trinity House, Charleston Road, Ranelagh, D06 C8X4 – Dublin, Ireland.

EMA/PDCO/569514/2022
Amsterdam, 24 June 2022

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

EMEA-003210-PIP01-22

Scope of the application

Active substance(s):

Doxecitine / doxribtimine

Condition(s):

Treatment of thymidine kinase 2 deficiency

Pharmaceutical form(s):

Powder for oral solution

Route(s) of administration:

Oral use

Gastric use

Name/corporate name of the PIP applicant:

Zogenix ROI Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Zogenix ROI Limited submitted for agreement to the European Medicines Agency on 17 March 2022 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 25 April 2022.

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 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 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 thymidine kinase 2 deficiency

2.1.1. Indication(s) targeted by the PIP

Treatment of thymidine kinase 2 deficiency with onset of symptoms on or before 12 years of age

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)

Powder for oral solution

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	**Study 1 (MT1621-19-008)** Definitive juvenile toxicity rat study to evaluate the toxicity and toxicokinetic characteristics of pyrimidine nucleosides doxecitine / doxribtimine.
Clinical studies	**Study 2 (MT-1621-102)** Open-label study to evaluate the efficacy, safety and pharmacokinetics of doxecitine / doxribtimine in children from birth to less than 18 years of age (and adults) with thymidine kinase 2 (TK2) deficiency.
Extrapolation, modelling and simulation studies	**Study 3** Population pharmacokinetic modelling study and exposure-response analysis to define and confirm the dose of doxecitine / doxribtimine to be used in children from birth to less than 18 years of age with thymidine kinase 2 (TK2) deficiency.
Other studies	**Study 4 (MT-1621-101)** Retrospective chart review study to evaluate the efficacy and safety of the combination of pyrimidine nucleosides in children from birth to less than 18 years of age (and adults) with thymidine kinase 2 (TK2) deficiency.

	Study 5 (MT-1621-107) Retrospective chart review study to evaluate and complement efficacy and safety data of the combination of pyrimidine nucleosides in children from birth to less than 18 years of age (and adults) with thymidine kinase 2 (TK2) deficiency not treated or treated with pyrimidine nucleoside therapy.
Other measures	Not applicable

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