EMA/113591/2014

European Medicines Agency decision

P/0071/2014

of 21 March 2014

on the agreement of a paediatric investigation plan and on the refusal of a waiver for cyclic pyranopterin monophosphate (monohydrobromide dihydrate) (EMEA-001491-PIP01-13) 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 Alexion Europe SAS on 10 June 2013 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 14 February 2014, in accordance with Article 18 of Regulation (EC) No 1901/2006, 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 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 refusing a waiver.

[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 cyclic pyranopterin monophosphate (monohydrobromide dihydrate), powder 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 waiver for cyclic pyranopterin monophosphate (monohydrobromide dihydrate), powder 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 refused.

Article 3

This decision is addressed to Alexion Europe SAS, 25 Boulevard de l'Amiral Bruix, 75016 – Paris, France.

Done at London, 21 March 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/733996/2013

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

EMEA-001491-PIP01-13

Scope of the application

Active substance(s):

Cyclic pyranopterin monophosphate (monohydrobromide dihydrate)

Condition(s):

Treatment of molybdenum cofactor deficiency type A

Pharmaceutical form(s):

Powder for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Alexion Europe SAS

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Alexion Europe SAS submitted for agreement to the European Medicines Agency on 10 June 2013 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 17 July 2013.

Supplementary information was provided by the applicant on 25 November 2013. 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 18 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 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 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 annex and appendix.

London, 14 February 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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

1. Waiver

1.1. Condition: treatment of molybdenum cofactor deficiency type A

The request for the waiver applied to:

- the paediatric population from 7 years to less than 18 years of age;
- for powder for solution for infusion, intravenous 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;
- (b) the disease or condition for which the specific medicinal product is intended occurs only in adult populations;
- (c) the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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 molybdenum cofactor deficiency type A

2.1.1. Indication(s) targeted by the PIP

Treatment of molybdenum cofactor deficiency type A

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 solution for infusion

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.

Area	Number of studies	Description
Non-clinical studies	2	Study 1: Juvenile toxicity study in rats, for 26-week treatment period and 28-day recovery period. Study 2: Juvenile toxicity study in dogs, for 9-month treatment period and 28-day recovery period.
Clinical studies	2	Study 3 (ALXN1101-MCD-201): Open-label, multicentre, dose-escalation study to evaluate the safety, activity and pharmacokinetics of cyclic pyranopterin monophosphate (ALXN1101) in children with a genetically confirmed diagnosis of Molybdenum cofactor deficiency type A, treated with recombinant Escherichia Coli-derived cyclic pyranopterin monophosphate. Study 4 (ALXN1101-MCD-202): Open-label, multicentre study to evaluate the safety and activity of cyclic pyranopterin monophosphate (ALXN1101) in children with a prenatal genetic diagnosis of Molybdenum cofactor deficiency type A, or who present with clinical signs and symptoms consistent with Molybdenum cofactor deficiency type A.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2019
Deferral for one or more measures contained in the paediatric investigation plan:	No