EMA/466415/2019

European Medicines Agency decision

P/0317/2019

of 11 September 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for fosmetpantotenate (EMEA-002036-PIP01-16) 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 Retrophin Europe Limited on 8 August 2016 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 26 July 2019, 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 granting 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 granting 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 fosmetpantotenate, powder for oral suspension, granules for oral suspension, oral 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 fosmetpantotenate, powder for oral suspension, granules for oral suspension, oral 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 fosmetpantotenate, powder for oral suspension, granules for oral suspension, oral 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 4

This decision is addressed to Retrophin Europe Limited, 2nd Floor, Palmerston House, Fenian Street, 2 - Dublin, Ireland.

EMA/PDCO/288259/2019 Corr
Amsterdam, 26 July 2019

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

EMEA-002036-PIP01-16

Scope of the application

Active substance(s):

Fosmetpantotenate

Condition(s):

Treatment of Pantothenate Kinase Associated Neurodegeneration

Pharmaceutical form(s):

Powder for oral suspension

Granules for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Retrophin Europe Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Retrophin Europe Limited submitted for agreement to the European Medicines Agency on 8 August 2016 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 13 September 2016.

Supplementary information was provided by the applicant on 23 April 2019. 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 grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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.

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

1.1. Condition

Treatment of Pantothenate Kinase Associated Neurodegeneration

The waiver applies to:

- the paediatric population from birth to less than 6 months of age ;
- powder for oral suspension, granules for oral suspension, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition

Treatment of Pantothenate Kinase Associated Neurodegeneration

2.1.1. Indication(s) targeted by the PIP

Treatment of Pantothenate Kinase Associated Neurodegeneration (PKAN)

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

From 6 months of age to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Powder for oral suspension

Granules for oral suspension

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1(FORM-DEV-1)** Confirmation of the suitability of the adult formulation for use in the paediatric population of patients less than 6 years of age. **Study 2 (FORM-DEV-2)** Development of an age appropriate formulation (taste-masked granule formulation) for use in children 6 months and above.
Non-clinical studies	2	**Study 3 (MPI 2223-026/RE-024-Report001-2016-TOX)** Identification of the dose(s) to be evaluated in the definitive juvenile toxicology study.

		Study 4 (MPI 2223-044/RE-024-Report063-2016-TOX) Evaluation of the potential toxicity when administered orally to juvenile rats (PND 22) for 10 weeks.
Clinical studies	3	**Study 5 (024PKAN15004)** Randomized, double-blind, placebo-controlled study to evaluate efficacy, safety and pharmacokinetics of fosmetpantotenate compared to placebo in patients 6 to less than 18 years of age (and adults), and to provide source data on PK/PD to support the extrapolation of efficacy in the target population of children from 6 months to less than 6 years of age with Pantothenate Kinase-associated Neurodegeneration (PKAN). **Study 6 (024PKAN19013)** Open-label, sequential dose cohort, two-part study to evaluate pharmacokinetics (PK), safety, tolerability, and activity of fosmetpantotenate and to provide PK/PD data to contribute to the extrapolation of efficacy (Part 1), with an extension to evaluate long term safety (Part 2). **Study 7** **(024PKAN15004 – open label extension part of Study 6)** Open label extension to evaluate long term efficacy and safety of fosmetpantotenate in patients 6 to less than 18 years of age (and adults) with PKAN following completion of double-blind period (Study 6).
Extrapolation, modelling and simulation studies	1	**Study 8** Modelling and simulation study to evaluate the dose of fosmetpantotenate in the treatment of patients 6 months to less than 6 years of age with PKAN based on existing population pharmacokinetics and efficacy data in adults and children 6 years of age and older with PKAN.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

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 August 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes