EMA/1822/2021

European Medicines Agency decision

P/0004/2021

of 14 January 2021

on the agreement of a paediatric investigation plan for (S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride (KH176) (EMEA-002113-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 Khondrion BV on 16 January 2017 under Article 16(1) of Regulation (EC) No 1901/2006,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 December 2020, in accordance with Article 17 of Regulation (EC) No 1901/2006,

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.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

[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 (S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride (KH176), age-appropriate oral liquid dosage form, 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

This decision is addressed to Khondrion BV, van Heemstraweg 49E, 6641 AA - Beuningen, Netherlands.

EMA/PDCO/524643/2020
Amsterdam, 11 December 2020

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

EMEA-002113-PIP01-16

Scope of the application

Active substance(s):

(S)-6-hydroxy-2,5,7,8-tetramethyl-N-((R)-piperidin-3-yl)chroman-2-carboxamide hydrochloride (KH176)

Condition(s):

Treatment of mitochondrial respiratory chain / oxidative phosphorylation defects

Pharmaceutical form(s):

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Khondrion BV

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Khondrion BV submitted for agreement to the European Medicines Agency on 16 January 2017 an application for a paediatric investigation plan for the above mentioned medicinal product.

The procedure started on 21 February 2017.

Supplementary information was provided by the applicant on 11 September 2020. The applicant proposed modifications to the paediatric investigation plan and requested a deferral.

During the procedure the applicant withdrew its request for a deferral.

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.

   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 mitochondrial respiratory chain / oxidative phosphorylation defects

2.1.1. Indication(s) targeted by the PIP

Treatment of mitochondrial disease caused by mitochondrial respiratory chain / oxidative phosphorylation defects

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)

Age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate formulation suitable for children from birth
Non-clinical studies	0	Not applicable
Clinical studies	2	**Study 2** Double-blind, randomised, placebo-controlled trial to evaluate pharmacokinetics, safety and efficacy of KH176 compared to placebo in children from birth to less than 18 years of age with genetically confirmed mitochondrial disease affecting oxidative phosphorylation and motor impairment **Study 3** Double-blind, randomised, placebo-controlled trial to evaluate safety and efficacy of KH176 compared to placebo in children from birth to less than 18 years of age with mitochondrial disease caused by oxidative phosphorylation system (OXPHOS) dysfunction and confirmed pathological mutation

Area	Number of measures	Description
Extrapolation, modelling and simulation studies	1	**Study 4** Modelling and simulation study to evaluate the use of KH176 in the treatment of mitochondrial disease caused by mitochondrial respiratory chain/oxidative phosphorylation defects in children from birth to less than 18 years of age with genetically confirmed mitochondrial disease
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 July 2024
Deferral for one or more measures contained in the paediatric investigation plan:	No