EMA/206268/2022

European Medicines Agency decision

P/0149/2022

of 13 May 2022

on the acceptance of a modification of an agreed 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-M01) 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 European Medicines Agency's decision P/0004/2021 issued on 14 January 2021,

Having regard to the application submitted by Khondrion BV on 2 December 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 25 March 2022, in accordance with Article 22 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 acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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

Changes to the agreed 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, capsule, hard, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Khondrion BV, Transistorweg 5C (M Building), 6534 AT – Nijmegen, The Netherlands.

EMA/PDCO/736459/2021 Corr
Amsterdam, 25 March 2022

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-002113-PIP01-16-M01

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

Capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Khondrion BV

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Khondrion BV submitted to the European Medicines Agency on 2 December 2021 an application for modification of the agreed paediatric investigation plan as set out in the European Medicines Agency's decision P/0004/2021 issued on 14 January 2021.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 31 January 2022.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

A new pharmaceutical form was added.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the 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

Capsule, hard

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate oral liquid dosage form suitable for children from birth **Study 5** Added during procedure EMEA-002113-PIP01-16-M01 Development of a hard capsule suitable for children from 6 years of age
Non-clinical studies	Not applicable
Clinical studies	**Study 2** (KH176-204) 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** (KH176-302) 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
Extrapolation, modelling and simulation studies	**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	Not applicable
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:	Yes
Date of completion of the paediatric investigation plan:	By June 2027
Deferral for one or more measures contained in the paediatric investigation plan:	No