EMA/18783/2022

European Medicines Agency decision

P/0030/2022

of 31 January 2022

on the acceptance of a modification of an agreed paediatric investigation plan for mitapivat (EMEA-002684-PIP01-19-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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on the acceptance of a modification of an agreed paediatric investigation plan for mitapivat (EMEA-002684-PIP01-19-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0365/2020 issued on 9 September 2020,

Having regard to the application submitted by Agios Netherlands B.V. on 10 September 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 17 December 2021, 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 and to the deferral.

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

Changes to the agreed paediatric investigation plan for mitapivat, film-coated tablet, age-appropriate oral solid dosage form, oral use, including changes to the deferral, 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 Agios Netherlands B.V., Zuidplein 36, Regus Amsterdam WTC, 1077XV – Amsterdam, The Netherlands.

EMA/PDCO/562891/2021 Corr
Amsterdam, 17 December 2021

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

EMEA-002684-PIP01-19-M01

Scope of the application

Active substance(s):

Mitapivat

Condition(s):

Treatment of pyruvate kinase deficiency

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Agios Netherlands B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Agios Netherlands B.V. submitted to the European Medicines Agency on 10 September 2021 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0365/2020 issued on 9 September 2020.

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

The procedure started on 19 October 2021.

Scope of the modification

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

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 and to the deferral 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 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 pyruvate kinase deficiency

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- film-coated tablet, oral use, age-appropriate oral solid dosage form, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of pyruvate kinase deficiency

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from 1 year to less than 18 years of age with pyruvate kinase deficiency

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

From 1 year to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral solid dosage form (coated granules) for use in paediatric patients unable to swallow the available tablets

Area	Number of measures	Description
Non-clinical studies	2	**Study 2** Dose range-finding juvenile toxicity study to determine tolerability of mitapivat and to provide information for the selection of dose levels in the definitive juvenile toxicity study (AG348-N-101) **Study 3** Definitive juvenile toxicity study to determine potential toxic effects of mitapivat on juvenile development and toxicokinetic characteristics of mitapivat and its metabolite, AGI-8702 (AG348-N-102).
Clinical studies	1	**Study 4** Randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of mitapivat in regularly transfused paediatric subjects with pyruvate kinase deficiency followed by a 5-year open-label extension period to evaluate safety.
Extrapolation, modelling and simulation studies	0	Not applicable.
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 February 2030.
Deferral for one or more measures contained in the paediatric investigation plan:	Yes