MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-100608-PIP01-22-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 (coated granules)

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Agios Netherlands B.V

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Agios Netherlands B.V submitted to the licensing authority on 22/07/2022 08:06 BST an application for a Modification

The procedure started on 08/08/2022 11:40 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100608-PIP01-22-M01

Of 22/08/2022 16:16 BST

On the adopted decision for mitapivat (MHRA-100608-PIP01-22-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for mitapivat, Film-coated tablet; Age-appropriate oral solid dosage form (coated granules) , ORAL USE .

This decision is addressed to Agios Netherlands B.V, Zuidplein 36, Regus Amsterdam WTC, Amsterdam, NETHERLANDS, 1077XV

ANNEX I

1. Waiver

1.1 Condition:

Treatment of pyruvate kinase deficiency The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Film-coated tablet; Age-appropriate oral solid dosage form (coated granules) Route(s) of administration: Oral use Reason for granting waiver: 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(s):

Treatment of pyruvate kinase deficiency

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients with pyruvate kinase deficiency

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 1 year to less than 18 years of age

2.4 Pharmaceutical Form(s):

Film-coated tablet; Age-appropriate oral solid dosage form (coated granules)

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	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.
Non-Clinical Studies	2	Study 2 (AG348-N-101) 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. Study 3 (AG348-N-102) Definitive juvenile toxicity study to determine potential toxic effects of mitapivat on juvenile development and toxicokinetic characteristics of mitapivat and its metabolite, AGI-8702.
Clinical Studies	1	Study 4 (AG348-C-022) 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, Modeling & Simulation Studies	0	Not applicable
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	28/02/2030
Deferral of one or more studies contained in the paediatric investigation plan:	Yes