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 (MHRA-100412-PIP01-22-M02) and to the deferral

MHRA-100412-PIP01-22-M03

Scope of the Application

Active Substance(s)

VADADUSTAT

Condition(s)

Treatment of anaemia due to chronic disorders

Pharmaceutical Form(s)

Film-coated tablet, Oral solution

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

MEDICE Arzneimittel Pütter GmbH & Co. KG

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, MEDICE Arzneimittel Pütter GmbH & Co. KG submitted to the licensing authority on 25/07/2024 11:52 BST an application for a Modification

The procedure started on 06/09/2024 10:38 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

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-100412-PIP01-22-M03

Of 28/10/2024 07:48 GMT

On the adopted decision for VADADUSTAT (MHRA-100412-PIP01-22-M03) 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 VADADUSTAT, Film-coated tablet, Oral solution , ORAL USE .

This decision is addressed to MEDICE Arzneimittel Pütter GmbH & Co. KG, Kuhloweg 37, Iserlohn, GERMANY, 58638

ANNEX I

1. Waiver

1.1 Condition:

Treatment of anaemia due to chronic disorders The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 4 months of age Pharmaceutical form(s): Film-coated tablet Oral solution Route(s) of administration: ORAL USE Reason for granting waiver: 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(s):

Treatment of anaemia due to chronic disorders

2.2 Indication(s) targeted by the PIP:

Treatment of anaemia secondary to chronic kidney disease

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

The paediatric population from 4 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Film-coated tablet Oral Solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate oral dosage form.
Non-Clinical Studies	2	Study 2 Pilot oral gavage study in juvenile rats. Study 3 This study was deleted in procedure EMEA-001944-PIP01-16-M01. Study 9 (added in procedure EMEA-001944-PIP01-16-M02 Definitive study in juvenile rats to determine the potential toxicity of vadadustat when administered daily to juvenile rats and to investigate the progression and/or reversibility of any treatment-related effects after a 6-week treatment free (recovery) period.
Clinical Studies	4	Study 4 Open-label, single-arm, externally controlled trial to evaluate the activity, safety, tolerability, PK and PD of oral vadadustat for the correction of anaemia in children from 4 months to less than 18 years of age with anaemia secondary to chronic kidney disease (CKD). Study 5 Medical record review study to assess the activity and safety of ESA treatment to correct and maintain haemoglobin levels in children from 4 months to less than 18 years of age with anaemia secondary to CKD and naïve to ESA treatment. Study 6 Open-label, single-arm,

		externally controlled trial to evaluate the activity, safety, tolerability, PK and PD of oral vadadustat for the maintenance treatment of anaemia in children from 4 months to less than 18 years of age with anaemia secondary to CKD receiving ESA treatment. Study 7 Medical record review study to assess the activity and safety of ESA treatment to maintain haemoglobin levels in children from 4 months to less than 18 years of age with anaemia secondary to CKD receiving ESA treatment.
Extrapolation, Modeling & Simulation Studies	1	Study 8 Modelling and simulation study to develop PK/PD simulations for the prediction of exposure and selection of doses to be used in children from 4 months to less than 18 years of age with anaemia secondary to CKD naïve to ESA treatment or receiving ESA treatment.
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:	31/05/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes