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-100250-PIP01-21-M01) and to the deferral

MHRA-100250-PIP01-21-M02

Scope of the Application

Active Substance(s)

VERICIGUAT

Condition(s)

Treatment of left ventricular failure

Pharmaceutical Form(s)

Age-appropriate oral liquid dosage form; Film-coated tablet

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Bayer plc

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Bayer plc submitted to the licensing authority on 07/10/2022 10:17 BST an application for a Modification

The procedure started on 09/03/2023 07:49 GMT

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-100250-PIP01-21-M02

Of 27/03/2023 07:41 BST

On the adopted decision for VERICIGUAT (MHRA-100250-PIP01-21-M02) 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 VERICIGUAT, Age-appropriate oral liquid dosage form; Film-coated tablet , ORAL USE .

This decision is addressed to Bayer plc, 400 South Oak Way, Reading, UNITED KINGDOM, RG2 6AD

ANNEX I

1. Waiver

1.1 Condition:

Treatment of left ventricular failure The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to 28 days of age Pharmaceutical form(s): Age-appropriate oral liquid dosage form Film-coated tablet 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 left ventricular failure

2.2 Indication(s) targeted by the PIP:

Treatment of symptomatic chronic heart failure with systemic left ventricular systolic dysfunction in paediatric patients 28 days to 18 years of age. Vericiguat reduces N terminal pro-hormone B-type natriuretic peptide (NT-proBNP) and is expected to improve cardiovascular outcomes.

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

The paediatric population older than 28 days to less than 18 years of age

2.4 Pharmaceutical Form(s):

Age-appropriate oral liquid dosage form Film-coated tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of a new age-appropriate oral liquid dosage form.
Non-Clinical Studies	2	Study 2 Establishment of dose levels for definitive juvenile toxicity study in rats (4-weeks study). Study 3 Evaluations of systemic toxicity of vericiguat in juvenile rats (13 weeks study).
Clinical Studies	3	Study 4 Deleted during procedure MHRA-100250-PIP01-21-M01. Study 5 Deleted during procedure MHRA-100250-PIP01-21-M01. Study 6 Relative bioavailability and food effect study in adult healthy subjects. Study 8 (Added during procedure MHRA-100250-PIP01-21-M01) Randomised, placebo-controlled, double-blind, multi-centre, adaptive, seamless trial to evaluate the safety, efficacy, and pharmacokinetics of vericiguat in paediatric participants older than 28 days to less than 18 years with symptomatic chronic heart failure due to left ventricular systolic dysfunction. Study 9 (Added during procedure MHRA-100250-PIP01-21-M01) Relative bioavailability and food effect study in adult healthy subjects of the oral liquid formulation.

Extrapolation, Modeling & Simulation Studies	1	Study 7 PBPK modelling study to predict the PK properties in the paediatric population.
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:	No
Date of completion of the paediatric investigation plan:	31/07/2030
Deferral of one or more studies contained in the paediatric investigation plan:	No