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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

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

MHRA-100084-PIP01-21-M02

Scope of the Application

Active Substance(s)

MIDOSTAURIN

Condition(s)

Treatment of acute myeloid leukaemia, Treatment of malignant mastocytosis, Treatment of mast cell leukaemia.

Pharmaceutical Form(s)

Capsule, soft, Oral solution

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Novartis Pharmaceuticals UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Novartis Pharmaceuticals UK Limited submitted to the licensing authority on 01/02/2024 18:13 GMT an application for a Modification

The procedure started on 18/04/2024 09:51 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-100084-PIP01-21-M02

Of 30/04/2024 11:54 BST

On the adopted decision for MIDOSTAURIN (MHRA-100084-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 MIDOSTAURIN, Capsule, soft, Oral solution , ORAL USE .

This decision is addressed to Novartis Pharmaceuticals UK Limited, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, , London, UNITED KINGDOM, W12 7FQ

ANNEX I

1. Waiver

1.1 Condition:

1.1 Condition: Treatment of acute myeloid leukaemia. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 3 months of age. Pharmaceutical form(s): Capsule, soft, Oral solution Route(s) of administration: ORAL USE Reason for granting waiver: On the grounds clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfill a therapeutic need of the specified paediatric subset(s). 1.2 Condition: Treatment of malignant mastocytosis. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 18 years of age. Pharmaceutical form(s): Capsule, soft, Oral solution Route(s) of administration: ORAL USE Reason for granting waiver: On the grounds the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s) 1.3 Condition: Treatment of mast cell leukaemia. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 18 years of age. Pharmaceutical form(s): Capsule, soft, Oral solution Route(s) of administration: ORAL USE Reason for granting waiver: On the grounds the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s)

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of acute myeloid leukaemia

2.2 Indication(s) targeted by the PIP:

Treatment of paediatric patients with FLT3 mutated AML, newly diagnosed.

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

The paediatric population from 3 months to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Capsule, soft Oral solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	1	Study 1 Juvenile development study.
Clinical Studies	2	Study 2 Open-label, dose-escalating, single-agent, multi-centre, age-stratified trial to evaluate toxicity, pharmacokinetics, pharmacodynamics, safety and activity of midostaurin in children from 3 months to less than 18 years of age with refractory or relapse acute lymphoblastic or acute myeloid leukaemia. Study 3 Open-label, dose-escalating, multi-centre trial to evaluate toxicity, pharmacokinetics, pharmacodynamics, safety and activity in children from 3 months to less than 18 years of age with newly-diagnosed acute myeloid leukaemia with FLT3 mutations.
Extrapolation, Modeling & Simulation Studies	1	Study 4 Population pharmacokinetic/ pharmacodynamic and outcome model to support extrapolation of efficacy.
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:	31/12/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes