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-100079-PIP01-21-M01) and to the deferral.

MHRA-100079-PIP01-21-M02

Scope of the Application

Active Substance(s)

GILTERITINIB FUMARATE

Condition(s)

Treatment of acute myeloid leukemia

Pharmaceutical Form(s)

Film-coated tablet Age appropriate oral dosage form

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Astellas Pharma Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Astellas Pharma Ltd submitted to the licensing authority on 03/03/2023 12:02 GMT an application for a Modification

The procedure started on 05/07/2023 09:32 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-100079-PIP01-21-M02

Of 23/08/2023 10:53 BST

On the adopted decision for GILTERITINIB FUMARATE (MHRA-100079-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 GILTERITINIB FUMARATE, Film-coated tablet Age appropriate oral dosage form , ORAL USE .

This decision is addressed to Astellas Pharma Ltd, 300 Dashwood Lang Road, Bourne Business Park, Addlestone, UNITED KINGDOM, KT15 2NX

ANNEX I

1. Waiver

1.1 Condition:

Treatment of acute myeloid leukaemia The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 6 months of age Pharmaceutical form(s): Film-coated tablet Age appropriate oral dosage form Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of acute myeloid leukaemia

2.2 Indication(s) targeted by the PIP:

Treatment of patients from 6 months to less than 18 years of age with relapsed or refractory FLT3/ ITD positive acute myeloid leukaemia or newly diagnosed FLT3/ITD positive acute myeloid leukaemia

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

The paediatric population from 6 months to less than 18 years of age

2.4 Pharmaceutical Form(s):

Film-coated tablet Age appropriate oral dosage form

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of film coated tablets smaller and of lower strength (compared to existing pharmaceutical form) and suitable to be administered as oral suspension and appropriate to children unable to swallow the adult sized film coated tablets.
Non-Clinical Studies	1	Study 2 Definitive juvenile rat study aimed to assess the toxicity of gilteritinib.
Clinical Studies	2	Study 3 (2215-CL-0603) Open-label, single arm, study to evaluate the pharmacokinetics, safety and anti-tumour activity of gilteritinib used in sequential combination with chemotherapy paediatric patients from 6 months to less than 18 years of age with FLT3/ ITD positive relapse or refractory acute myeloid leukaemia (AML) with a dose finding phase (phase 1)and an expansion phase (phase 2). Study 4 (2215-CL-0604: gilteritinib in combination with standard chemotherapy arm) Open label, single-arm phase 2 study to evaluate the pharmacokinetics, safety and efficacy of gilteritinib used in sequential combination with chemotherapy in paediatric patients from 6 months to less than 18 months

		of age (and young adults) with newly diagnosed, FLT3/ITD positive, AML.
Extrapolation, Modeling & Simulation Studies	2	Study 5 Modelling and simulation study to simulate and predict gilteritinib exposure in children from 6 months to less than 18 years of age with acute myeloid leukaemia. Study 6 (added in Modification MHRA-100079-PIP01-21-M01) Physiologically based modelling study to simulate gilteritinib exposure in populations of children from 6 months to less than 18 years of age with AML.
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:	30/09/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes