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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral and grant a waiver

MHRA-100345-PIP01-21

Scope of the Application

Active Substance(s)

Magrolimab

Condition(s)

Treatment of myelodysplastic syndromes (including juvenile myelomonocytic leukaemia), Treatment of acute myeloid leukaemia

Pharmaceutical Form(s)

Concentrate for solution for infusion; Age-appropriate dosage formulation for parenteral use

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Gilead Sciences Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Gilead Sciences Ltd submitted to the licensing authority on 23/06/2022 18:06 BST an application for a Paediatric Investigation Plan

The procedure started on 12/12/2022 12:53 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 agree a paediatric investigation plan and grant a deferral and grant a waiver

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-100345-PIP01-21

Of 19/01/2023 14:18 GMT

On the adopted decision for Magrolimab (MHRA-100345-PIP01-21) 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 a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for Magrolimab, Concentrate for solution for infusion; Age-appropriate dosage formulation for parenteral use , INTRAVENOUS USE .

This decision is addressed to Gilead Sciences Ltd, 280 High Holborn, London, UNITED KINGDOM, WC1V 7EE

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of myelodysplastic syndromes (including juvenile myelomonocytic leukaemia) Condition2 : Treatment of acute myeloid leukaemia For both Conditions, the waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 28 days of age Pharmaceutical form(s): Concentrate for solution for infusion Age-appropriate dosage formulation for parenteral use Route(s) of administration: INTRAVENOUS 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):

Condition 1: Treatment of myelodysplastic syndromes (including juvenile myelomonocytic leukaemia) Condition2 : Treatment of acute myeloid leukaemia

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of paediatric patients from 28 days to less than 18 years of age with advanced myelodysplastic syndromes or with advanced juvenile myelomonocytic leukaemia.
Condition2 : Treatment of paediatric patients from 28 days to less than 18 years of age with refractory or relapsed acute myeloid leukaemia or with newly diagnosed acute myeloid leukaemia.

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

For both Conditions: The paediatric population from 28 days to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both Conditions: Concentrate for solution for infusion Age-appropriate dosage formulation for parenteral use

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of a dosage formulation for parenteral use appropriate for all paediatric patients from 28 days to less than 18 years of age.
Non-Clinical Studies	4	Study 3 In vitro phagocytosis study to evaluate the efficacy of magrolimab monotherapy and in combination with azacitidine in paediatric acute myeloid leukaemia patient cell lines.Study 2 (Study 2a) In vitro phagocytosis study to evaluate the efficacy of magrolimab monotherapy and in combination with azacitidine in primary juvenile myelomonocytic leukaemia patient cell lines. Study 4 (Study 2c) In vivo study to evaluate the efficacy of magrolimab monotherapy and in combination with azacitidine in a validated patient-derived xenograft mouse model of juvenile myelomonocytic leukaemia. Study 5 (Study 2d) In vivo study in a genetic mouse model to evaluate inhibition or elimination of juvenile

		myelomonocytic leukaemia cancer cells with magrolimab alone, azacitidine alone and magrolimab in combination with azacitidine.
Clinical Studies	4	Study 6 (Paediatric study- Phase 1) Open-label, single-arm study to evaluate the safety, pharmacokinetics (PK), and preliminary anti-tumour activity of magrolimab used in combination with azacitidine for paediatric patients from 28 days to less than 18 years of age with newly diagnosed advanced myelodysplastic syndromes (MDS) or newly diagnosed advanced juvenile myelomonocytic leukaemia (JMML) or relapsed/refractory acute myeloid leukaemia (AML). Study 7 (Paediatric study- Phase 2, Arm 1) Open label, single-arm study to evaluate and confirm the safety and anti-tumour activity of magrolimab used in combination with azacitidine in paediatric patients from 28 days to less than 18 years of age with newly diagnosed advanced MDS or newly diagnosed advanced JMML. Study 8 (Paediatric study -Phase 2 Arm 2) Open-label, single arm study to evaluate and confirm the safety and anti-tumour activity of magrolimab used in combination with azacitidine in paediatric patients from 28 days to less than 18 years of age with relapsed/refractory acute myeloid leukaemia (AML). Study 9 Open label, randomised controlled study to evaluate the safety, pharmacokinetics and efficacy of magrolimab used in combination with azacitidine as compared to standard of care in paediatric patients from 28 days to less than 18 years of age with newly diagnosed acute myeloid leukaemia (AML).
Extrapolation, Modeling & Simulation Studies	2	Study 10 Modelling and simulation study to simulate exposure and to determine the dose of magrolimab to be used in combination with azacitidine in children from 28 days to less than 18 years of age with newly diagnosed advanced myelodysplastic syndromes (MDS)

		or newly diagnosed advanced juvenile myelomonocytic leukaemia (JMML) or relapsed/ refractory acute myeloid leukaemia (AML). Study 11 Extrapolation study to support the use of magrolimab in combination with azacitidine in paediatric patients from 28 days to less than 18 years of age with newly diagnosed advanced MDS.
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:	30/09/2035
Deferral of one or more studies contained in the paediatric investigation plan:	Yes