EMA/623897/2021

European Medicines Agency decision

P/0531/2021

of 3 December 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for magrolimab (EMEA-002819-PIP01-20) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Gilead Sciences International Ltd on 7 August 2020 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 October 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for magrolimab, concentrate for solution for infusion, age appropriate dosage formulation for parenteral use, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for magrolimab, concentrate for solution for infusion, age appropriate dosage formulation for parenteral use, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for magrolimab, concentrate for solution for infusion, age appropriate dosage formulation for parenteral use, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Gilead Sciences International Ltd, Flowers Building, Granta Park, Abington, CB21 6GT – Cambridge, United Kingdom.

EMA/PDCO/417280/2021
Amsterdam, 15 October 2021

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-002819-PIP01-20

Scope of the application

Active substance(s):

Magrolimab

Condition(s):

Treatment of acute myeloid leukaemia

Treatment of myelodysplastic syndromes (including juvenile myelomonocytic 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 International Ltd

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Gilead Sciences International Ltd submitted for agreement to the European Medicines Agency on 7 August 2020 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 15 September 2020.

Supplementary information was provided by the applicant on 9 July 2021.The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of acute myeloid leukaemia

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- concentrate for solution for infusion, age appropriate dosage formulation for parenteral use, intravenous use;
- 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).

1.2. Condition:

Treatment of myelodysplastic syndromes (including juvenile myelomonocytic leukaemia)

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- concentrate for solution for infusion, age appropriate dosage formulation for parenteral use, intravenous use;
- 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:

Treatment of acute myeloid leukaemia

2.1.1. Indication(s) targeted by the PIP

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

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

Age appropriate dosage formulation for parenteral use

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	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	1	**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 2b).
Clinical studies	3	**Study 6** Open label, single-arm study to evaluate the safety, pharmacokinetics and preliminary 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 myelodysplastic syndrome (MDS) or newly diagnosed advanced juvenile myelomonocytic leukaemia (JMML) or relapsed/refractory acute myeloid leukaemia (AML) (Paediatric study- Phase 1). **Study 8** 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) (Paediatric study- Phase 2, Arm 2). **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, modelling and simulation studies	1	**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 syndrome (MDS) or newly diagnosed advanced juvenile myelomonocytic leukaemia (JMML) or relapsed/refractory acute myeloid leukaemia (AML).
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of myelodysplastic syndromes (including juvenile myelomonocytic leukaemia)

2.2.1. Indication(s) targeted by the PIP

Treatment of paediatric patients from 28 days to less than 18 years of age with advanced myelodysplastic syndromes or with advanced juvenile myelomonocytic leukaemia.

2.2.2. Subset(s) of the paediatric population concerned by the paediatric development

From 28 days to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Concentrate for solution for infusion

Age appropriate dosage formulation for parenteral use

2.2.4. Measures

Area	**Number of measures**	**Description**
Quality-related studies	1	**Study 1** Same as Study 1 for condition treatment of acute myeloid leukaemia.
Non-clinical studies	3	**Study 2** 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 2a). **Study 4** In *vivo* study to evaluate the efficacy of magrolimab monotherapy and combination with azacitidine in a validated patient-derived xenograft mouse model of juvenile myelomonocytic leukaemia (Study 2c). **Study 5** 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 azacytidine (Study 2d).
Clinical studies	2	**Study 6** (Paediatric study- Phase 1) same as Study 6 for condition treatment of acute myeloid leukaemia. **Study 7** 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 myelodysplastic syndrome (MDS) or newly diagnosed advanced juvenile myelomonocytic leukaemia (JMML) (Paediatric study- Phase 2, Arm 1).
Extrapolation, modelling and simulation studies	2	**Study 10** same as Study 10 for condition treatment of acute myeloid leukaemia. **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 myelodysplastic syndrome (MDS).
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By September 2035
Deferral for one or more measures contained in the paediatric investigation plan:	Yes