



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/369846/2019

European Medicines Agency decision P/0234/2019

of 16 July 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human β A-T87Q-globin gene (LentiGlobin BB305) (EMEA-001665-PIP02-17) 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.

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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 726/2004¹,

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 Agency²,

Having regard to the application submitted by bluebird bio France on 23 October 2017 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 29 May 2019, 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 autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human β A-T87Q-globin gene (LentiGlobin BB305), dispersion for infusion, 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 autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human β A-T87Q-globin gene (LentiGlobin BB305), dispersion for infusion, 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 autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human β A-T87Q-globin gene (LentiGlobin BB305), dispersion for infusion, 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/0257/2015 issued on 30 October 2015, including subsequent modifications thereof.

Article 5

This decision is addressed to bluebird bio France, 155 rue de Faubourg, Saint-Denis, 75010 - Paris, France.

EMA/PDCO/177770/2019
Amsterdam, 29 May 2019

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

EMA-001665-PIP02-17

Scope of the application

Active substance(s):

Autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human β A-T87Q-globin gene (LentiGlobin BB305)

Condition(s):

Treatment of sickle cell disease

Pharmaceutical form(s):

Dispersion for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

bluebird bio France

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, bluebird bio France submitted for agreement to the European Medicines Agency on 23 October 2017 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 28 November 2017.

Supplementary information was provided by the applicant on 25 February 2019. 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 sickle cell disease

The waiver applies to:

- the paediatric population weighing less than 6 kg;
- dispersion for infusion, intravenous use;
- 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:

Treatment of sickle cell disease

2.1.1. Indication(s) targeted by the PIP

Treatment of sickle cell disease

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

From 6 kg of weight to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Dispersion for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	4	Study 1 (HGB-205) Open label study to evaluate the safety, success of engraftment and efficacy of gene therapy of the beta-haemoglobinopathies [severe sickle cell anaemia (sickle cell disease; SCD) or beta-thalassemia major] by transplantation of autologous CD34+ stem cells transduced <i>ex vivo</i> with a lentiviral beta-A-T87Q globin vector (LentiGlobin BB305) in children from 5 years to

		less than 18 years of age (and adults). Study 2 (HGB-206) Open label, non-randomised, single dose study to evaluate hematopoietic stem cell (HSC) transplantation (HSCT) using LentiGlobin BB305 in subjects from 12 years to less than 18 years of age (and adults) with severe SCD. Study 3 (HGB-210) Open label, single-arm, single dose trial to evaluate efficacy and safety of autologous CD34⁺ haematopoietic stem cells transduced with lentiviral vector encoding the human beta^{A-T87Q}-globin gene (LentiGlobin BB305) in patients weighing at least 6 kg and less than 18 years of age (and adults) with sickle cell disease (SCD) Study 4 (HGB-211) Open label, single-arm, single dose study to evaluate efficacy and safety of LentiGlobin BB305 in patients weighing at least 6 kg and less than 15 years of age with SCD and at elevated risk of stroke despite chronic blood transfusions
Extrapolation, modelling and simulation studies	0	Not applicable
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:	Yes
Date of completion of the paediatric investigation plan:	By December 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes