EMA/206734/2022

European Medicines Agency decision

P/0175/2022

of 13 May 2022

on the refusal of a modification of an agreed paediatric investigation plan for betibeglogene autotemcel (Zynteglo), (EMEA-001665-PIP01-14-M06) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0257/2015 issued on 30 October 2015, the decision P/0297/2016 issued on 4 November 2016, the decision P/0067/2018 issued on 16 March 2018, the decision P/0020/2020 of 6 January 2020, the decision P/0008/2021 issued on 15 January 2021 and the decision P/0232/2021 issued on 16 June 2021,

Having regard to the application submitted by Bluebird bio (Netherlands) B.V. on 16 December 2021 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 25 March 2022, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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 refusal of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the refusal of changes to the agreed paediatric investigation plan, including changes to the deferral.

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for betibeglogene autotemcel (Zynteglo), dispersion for infusion, intravenous use, including changes to the deferral, 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, are hereby refused.

Article 2

This decision is addressed to Bluebird bio (Netherlands) B.V., 7 Stadsplateau WTC Utrecht, 3521AZ – Utrecht, The Netherlands.

EMA/PDCO/3177/2022
Amsterdam, 25 March 2022

Opinion of the Paediatric Committee on the refusal of a modification of an agreed Paediatric Investigation Plan

EMEA-001665-PIP01-14-M06

Scope of the application

Active substance(s):

Betibeglogene autotemcel

Invented name:

Zynteglo

Condition(s):

Treatment of beta-thalassaemia

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Dispersion for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Bluebird bio (Netherlands) B.V.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bluebird bio (Netherlands) B.V. submitted to the European Medicines Agency on 16 December 2021 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0257/2015 issued on 30 October 2015, the decision P/0297/2016 issued on 4 November 2016, the decision P/0067/2018 issued on 16 March 2018, the decision P/0020/2020 of 6 January 2020, the decision P/0008/2021 issued on 15 January 2021 and the decision P/0232/2021 issued on 16 June 2021.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 31 January 2022.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends, as set out in the appended summary report:

   - to refuse the changes proposed by the applicant regarding the paediatric investigation plan and the deferral.

   The Paediatric Committee member of Norway 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 remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes 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 beta-thalassaemia

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 beta-thalassaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of beta-thalassaemia major and severe intermedia

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	3	**Study 1** Open-label, non-randomised, single dose trial with 2 cohorts to evaluate activity and safety of autologous CD34+ haematopoietic stem cells transduced with lentiviral vector encoding the human betaA-T87Q-globin gene (LentiGlobin BB305) in adolescents from 12 years to less than 18 years of age (and adults) with transfusion-dependent beta-thalassaemia (TDT) who do not have a $beta^0$ mutation at both alleles of the beta-globin (HBB) gene [Cohort 1] and in children weighing at least 6 kg and

		less than 12 years of age with TDT who do not have a beta^0 mutation at both alleles of the HBB gene [Cohort 2]. (HGB-207) **Study 2** *This study has been deleted in procedure EMEA-001665-PIP01-14-M01.* **Study 3** Open-label, non-randomised, single dose trial to evaluate efficacy and safety of LentiGlobin BB305 in children from 2 to less than 18 years of age (and adults) who received 4-7 transfusions in the prior year. (HGB-209) **Study 4** Open-label, non-randomised, single dose trial to evaluate activity and safety of LentiGlobin BB305 in adolescents and children weighing at least 6 kg and less than 18 years of age (and adults) with transfusion-dependent beta thalassaemia (TDT). (HGB-212)
Extrapolation, modelling and simulation studies	1	**Study 5** Comprehensive analysis of in-house clinical studies with TDT patients including adults and children as well as historic data to contextualise and pool with (as applicable) the data generated in patients receiving 4-7 transfusions a year through study 3 (HGB-209)
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 September 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of beta-thalassaemia

Authorised indication(s):

- Zynteglo is indicated for the treatment of patients 12 years and older with transfusion-dependent β-thalassaemia (TDT) who do not have a β0/β0 genotype, for whom haematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available.

Authorised pharmaceutical form(s):

Dispersion for infusion

Authorised route(s) of administration:

Intravenous use