MHRA
10 South Colonnade
Canary Wharf
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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-100169-PIP01-21-M01

Scope of the Application

Active Substance(s)

BETIBEGLOGENE AUTOTEMCEL

Condition(s)

Treatment of beta-thalassaemia

Pharmaceutical Form(s)

Dispersion for infusion

Route(s) of Administration

Intravenous use

Name / Corporate name of the PIP applicant

Bluebird bio (Netherlands) B.V.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Bluebird bio (Netherlands) B.V. submitted to the licensing authority on 12/07/2021 18:21 BST an application for a Modification

The procedure started on 04/07/2022 11:26 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

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-100169-PIP01-21-M01

Of 25/11/2022 08:54 GMT

On the adopted decision for BETIBEGLOGENE AUTOTEMCEL (MHRA-100169-PIP01-21-M01) 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 BETIBEGLOGENE AUTOTEMCEL, Dispersion for infusion , Intravenous use .

This decision is addressed to Bluebird bio (Netherlands) B.V., bluebird bio (Netherlands) B.V, Stadsplateau 7, WTC Utrecht, Utrecht, Netherlands, 3511AZ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of beta-thalassaemia The waiver applies / applied to: Paediatric Subset(s): The paediatric population weighing less than 6 kg Pharmaceutical form(s): Dispersion for infusion Route(s) of administration: Intravenous use Reason for granting waiver: 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(s):

Treatment of beta-thalassaemia

2.2 Indication(s) targeted by the PIP:

Treatment of beta-thalassaemia major and severe intermedia

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

The paediatric population from 6 kg body weight to less than 18 years of age

2.4 Pharmaceutical Form(s):

Dispersion for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	0	Not applicable
Clinical Studies	3	Study 1 (HGB-207) 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 beta0 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 beta0 mutation at both alleles of the HBB gene [Cohort 2]. Study 2 This study was deleted in procedure EMEA-001665-PIP01-14-M01. Study 3 (HGB-209) Open-label, non-randomised, single dose trial to evaluate efficacy and safety of LentiGlobin BB305 in children from 2 years to less than 18 years of age (and adults) who received 4-7 transfusions in the prior year. Study 4 (HGB-212) 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).
Extrapolation, Modeling & Simulation Studies	1	Study 5 (HGB-209) 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.
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