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ZYNTEGLO (Betibeglogene autotemcel**)**

All KY Medicaid members (MCO and FFS) are subject to the same criteria. For MCO members, please submit requests along with clinical information to the MCO for review. For FFS members, please submit requests along with clinical information to dmspharmacy@ky.gov.

FDA Approved Indication(s)

Betibeglogene autotemcel (Zynteglo) is an autologous hematopoietic stem cell-based gene therapy for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions.

Policy/Criteria

I. Initial Approval

Provider must submit documentation (such as office chart notes, lab results, or other clinical information) supporting that the member has met all approval criteria. Initial approval is for 12 months.

- Prescribed by or in consultation with a hematologist or transplant specialist or other appropriate specialist in the treatment of β-thalassemia**; and**
- Diagnosis of transfusion-dependent β-thalassemia with a non β 0/ β 0 or β 0/ β 0 genotype confirmed by genetic testing. (Please reference Appendix A for examples.); **and**
- The member is ≥ 4 years of age with a weight of at least 6 kg**; and**
- Documentation of one of the following:
  - Receipt of ≥8 transfusions of packed red blood cells (pRBC) per year in the previous two years; **or**
  - Receipt of at least 100 mL/kg/year of pRBCs in the previous two years; **and**
- Documentation to verify the following:

- The member has a negative lab value within the past 6 months for HIV1 and 2; human T-lymphotropic virus 1&2 (HTLV1&HTLV2), Hepatitis B virus and hepatitis C virus before the cell collection.
- The member does not have any prior or current malignancy (with the exception of adequately treated cone biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin) or myeloproliferative or significant immunodeficiency disorder;
- The member can provide an adequate number of cells to meet the minimum recommended dose of 5.0x10^6 CD34+ cells/kg;
- The member has not received prior allogeneic hematopoietic stem cell transplantation; **and**

- Females of childbearing potential and males capable of fathering a child: Member has been counseled on the use of effective contraception during treatment (from start of mobilization through at least 6 months after administration of Zynteglo) and advised of the risks associated with conditioning agents; **and**

- Females of childbearing potential must not be pregnant or breastfeeding, **AND** must have a documented negative serum pregnancy test within the past 30 days
  NOTE: A negative serum pregnancy test must be confirmed before the start of mobilization and then confirmed again before conditioning procedures and before Zynteglo administration; **and**

- The member has not received a prior dose of Zynteglo or other gene therapy, or is being considered for other gene therapy or investigational cellular therapy for B-thalassemia**; and**

- Provider attests the dose contains a minimum of 5.0 x 10^6 CD34+ cells/kg.

II. Continuation of Therapy:

This cannot be reviewed since the product is currently indicated for a one-dose per lifetime administration.

III. Appendices

Appendix A: Genetic Confirmation of β-thalassemia

β-thalassemia Genotypes
β^0/β^0
β^0/β^+
β^+/β^+
β^E/β^0
β^+ IVS1-110/β^+ IVS1-110
β^0/β^+ IVS1-110

REFERENCES

1. Zynteglo Prescribing Information. Somerville, MA: bluebird bio, Inc.; August 2022. Available at: https://www.bluebirdbio.com/-/media/bluebirdbio/CorporateCOM/Files/Zynteglo/ZYNTEGLO_Prescribing_Information.pdf. Accessed March 22, 2025.

2. ClinicalTrials.gov. A study evaluating the efficacy and safety of the Lentiglobin® BB305 drug product in subjects with transfusion-dependent β-thalassemia, who do not have a β0/β0 genotype. Last updated June 25, 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT02906202. March 22, 2025.

3. ClinicalTrials.gov. A study evaluating the efficacy and safety of the Lentiglobin® BB305 drug product in subjects with transfusion-dependent β-thalassemia. Last updated June 24, 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT03207009. Accessed March 22, 2025.

4. Locatelli F, Thompson AA, Kwiatkowski JL, et al. Betibeglogene autotemcel gene therapy for non-β0/β0 genotype β-thalassemia. N Engl J Med. 2022;386(5):415-427.

5. Porter JB, Thompson AA, Walters MC, et al. Improvement in erythropoiesis in patients with transfusion dependent β-thalassemia following treatment with betibeglogene autotemcel (LentiGlobin for β-thalassemia) in the phase 3 HGB-207 study. EHA 2020 Virtual Congress Abstract: S296.

6. Cappellini MD, Farmakis D, Porter J, et al. Guidelines for the management of transfusion dependent thalassemia (TDT) 4th Edition. Thalassemia International Federation (2021). Available at: https://thalassaemia.org.cy/publications/tif-publications/guidelines-for-the-management-of-transfusion-dependent-thalassaemia-4th-edition-2021/. Accessed March 22, 2025.