Betibeglogene autotemcel (Zynteglo®) (Intravenous)

IMPORTANT REMINDER
We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Zynteglo is indicated for the treatment of adult and pediatric patients with beta-thalassemia who require regular blood cell (RBC) transfusions.

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
- Molecular or genetic testing results documenting transfusion-dependent beta-thalassemia genotype.
- Chart notes or medical record documenting history of blood cell transfusions for the previous two years.

PRESCRIBER SPECIALITIES

This medication must be prescribed by or in consultation with a hematologist.

COVERAGE CRITERIA

Transfusion-Dependent Beta-Thalassemia

Authorization of 3 months for one dose total may be granted for transfusion-dependent beta thalassemia when all of the following criteria are met:
- Member is 4 years of age or older and meets both of the following criteria:
  - Member weighs at least 6 kg.
  - Member is reasonably anticipated to provide at least the minimum number of cells required to initiate the manufacturing process
- Member has a diagnosis of transfusion-dependent beta-thalassemia with a non-β0/β0 OR β0/β0 genotype confirmed via genetic testing (see Appendix for examples).
- Member requires regular blood cell transfusions and meets one of the following criteria within the previous two years:
  - Member has received at least 100 milliliter per kilogram of packed red blood cells (pRBCs) per year.
  - Member has received at least 8 transfusions events of packed red blood cells (pRBCs) per year.

- Member is eligible for a hematopoietic stem cell transplant (HSCT) but is unable to find a matched (10/10) human leukocyte antigen (HLA) related donor.
- Member has not received a prior hematopoietic stem cell transplant (HSCT).
- Member has not received Zynteglo or any other gene therapy previously.
- Member does not have any of the following conditions:
  - Severe iron overload (e.g., T2*-weighted magnetic resonance imaging [MRI] measurements of myocardial iron less than 10 msec).
  - Positive for the presence of human immunodeficiency virus type 1 or 2 (HIV-1 and HIV-2), hepatitis B virus (HBV), or hepatitis C (HCV).
  - Any prior or current malignancy.
  - Advanced liver disease (e.g., bridging fibrosis, cirrhosis, active hepatitis).
  - Uncorrected bleeding disorder.
  - Myeloproliferative and/or immunodeficiency disorder.
  - Uncontrolled seizure disorder.
  - Renal impairment (e.g., estimated glomerular filtration rate ≤ 70 mL/min/1.73 m2).

APPENDIX

Examples of non-β0/β0 OR β0/β0 genotypes:

- β0/β0
- β0/β+
- βE/β0
- β0/IVS-I-110
- IVS-I-110/IVS-1-110

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

RRFERENCES

1. Zynteglo [package insert]. Somerville, MA: Bluebird Bio; August 2022.
2. 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.
3. Ashutosh Lal, Franco Locatelli, Janet L. Kwiatkowski, Andreas E. Kulozik, Evangelia Yannaki, John B. Porter, Isabelle Thuret, Martin G. Sauer, Heidi Elliot, Ying Chen, Richard A. Colvin, Alexis A. Thompson; Northstar-3: Interim Results from a Phase 3 Study Evaluating Lentiglobin Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia and Either a β0 or IVS-I-110 Mutation at Both Alleles of the HBB Gene. Blood 2019; 134 (Supplement_1): 815.
4. Cappellini MD, Farmakis D, Porter J, Taher A. 2021 Guidelines for the management of transfusion dependent thalassaemia (TDT). Nicosia, Cyprus: Thalassaemia International Federation, 2021.

BlueCross BlueShield of Tennessee

Policy

Medical Policy Manual **Approved Rev: Do Not Implement until 4/2/26**

EFFECTIVE DATE 4/2/2026

ID_CHS_2025