Reference number(s)
5544-A

Specialty Guideline Management
Zynteglo

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Zynteglo	betibeglogene autotemcel

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[1]

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 Specialties

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

Coverage Criteria

Transfusion-Dependent Beta-Thalassemia[1-4]

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 m^2).

Appendix[1-3]

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

References

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.