

SPECIALTY GUIDELINE MANAGEMENT

ZYNTEGLO (betibeglogene autotemcel)

POLICY

I. 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.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

- A. Molecular or genetic testing results documenting transfusion-dependent beta-thalassemia genotype
- B. Chart notes or medical record documenting history of blood cell transfusions for the previous two years

III. PRESCRIBER SPECIALTIES

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

IV. CRITERIA FOR INITIAL APPROVAL

Beta-thalassemia

Authorization of 3 months for a one-time administration may be granted when all of the following criteria are met:

- A. Member is 4 years of age or older and meets both of the following criteria:
 - 1. Member weighs at least 6 kg
 - 2. Member is reasonably anticipated to provide at least the minimum number of cells required to initiate the manufacturing process
- B. Member has a diagnosis of transfusion-dependent beta-thalassemia with a non- β^0/β^0 OR β^0/β^0 genotype confirmed via genetic testing (Appendix A)
- C. Member requires regular blood cell transfusions and meets one of the following criteria within the previous two years:
 - 1. Member has received at least 100 milliliter per kilogram of packed red blood cells (pRBCs) per year
 - 2. Member has received at least 8 transfusions events of packed red blood cells (pRBCs) per year
- D. Member is eligible for a hematopoietic stem cell transplant (HSCT) but is unable to find a matched related donor
- E. Member has not received prior hematopoietic stem cell transplant (HSCT)
- F. Member has not received Zynteglo or any other gene therapy previously

- G. Member does not have any of the following conditions:
1. 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)
 2. Any prior or current malignancy
 3. Advanced liver disease (e.g., bridging fibrosis, cirrhosis, active hepatitis)
 4. Severely elevated iron in the heart (i.e., patients with cardiac T2* less than 10 msec by MRI)

V. APPENDIX

Examples of non- β^0/β^0 OR β^0/β^0 genotypes:

1. β^0/β^0
2. β^0/β^+
3. β^E/β^0
4. $\beta^0/IVS-I-110$
5. $IVS-I-110/IVS-I-110$

VI. 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- β^0/β^0 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 β^0 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.