CareSource

PHARMACY POLICY STATEMENT
North Carolina Marketplace

DRUG NAME	Zynteglo (betibeglogene autotemcel)
BILLING CODE	J3590
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Zynteglo ("beti-cel") is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusion. It is a one-time, single dose suspension of CD34+ cells for IV infusion. The patient's stem cells are collected and transduced ex vivo with a vector encoding functional copies of a modified form of the beta-globin gene (HbAT87Q) and then re-infused back into the patient.
Beta-thalassemia is a rare blood disorder caused by mutations in the beta-globin (HBB) gene which lead to absent (β^0) or reduced (β^+) production of functional adult hemoglobin (HbA), impeding RBC development and survival (ineffective erythropoiesis) to result in microcytic anemia, iron overload, and other complications. The most severely affected patients have lifelong dependency on RBC transfusions and require iron chelation.
The pivotal phase 3 studies for Zynteglo are Northstar-2 and Northstar-3. The pooled data showed that 89% of the evaluable patients achieved transfusion independence (TI), defined as no longer needing RBC transfusion for at least 12 months while maintaining an average hemoglobin level of at least 9. Patients are being followed for 15 years in an extension study.

Zynteglo (betibeglogene autotemcel) will be considered for coverage when the following criteria are met:

Beta-Thalassemia

For **initial** authorization:

1. Member is at least 4 years of age (and weighs at least 6 kg); AND
2. Medication must be prescribed by or in consultation with a hematologist or transplant specialist; AND
3. Member has a diagnosis of transfusion-dependent β-thalassemia (TDT), defined as at least 100 mL/kg/year of pRBCs in the last 2 years or at least 8 transfusions of pRBCs per year in the last 2 years; AND
4. Member is clinically stable and a suitable candidate for allogenic HSCT but does NOT have an available and willing human leukocyte antigen (HLA) matched sibling/family donor; AND
5. Member has tested negative for Hepatitis B, Hepatitis C, HIV, and human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2) before cell collection; AND
6. Member does NOT have any of the following:
    a. Prior or current malignancy
    b. Prior HSCT
    c. Prior gene therapy
    d. Advanced liver disease
    e. Cardiac T2* <10 ms on MRI (indicates iron overload in the heart).

7. **Dosage allowed/Quantity limit**: Minimum 5.0 × 10^6 CD34+ cells/kg.
   Limit: 80 mL (4 bags)

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Zynteglo will not be authorized for continued therapy.

CareSource considers Zynteglo (betibeglogene autotemcel) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
09/19/2022	New policy for Zynteglo created.

References:

1. Zynteglo [prescribing information]. bluebird bio, Inc.; 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. doi:10.1056/NEJMoa2113206
3. Thompson AA, Walters MC, Kwiatkowski J, et al. Gene Therapy in Patients with Transfusion-Dependent β-Thalassemia. *N Engl J Med*. 2018;378(16):1479-1493. doi:10.1056/NEJMoa1705342
4. Farmakis D, Porter J, Taher A, Domenica Cappellini M, Angastiniotis M, Eleftheriou A. 2021 Thalassaemia International Federation Guidelines for the Management of Transfusion-dependent Thalassemia. *Hemasphere*. 2022;6(8):e732. Published 2022 Jul 29. doi:10.1097/HS9.0000000000000732

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