Corporate Medical Policy: Betibeglogene autotemcel (Zynteglo®) **"Notification"** **POLICY EFFECTIVE APRIL 1, 2026**

Restricted Product(s):

- betibeglogene autotemcel (Zynteglo®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- For treatment of adult and pediatric patients with ß-thalassemia who require regular red blood cell (RBC) transfusions

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The patient has a diagnosis of transfusion dependent beta-thalassemia (β-thalassemia major or TDT) **[medical record documentation required]**; **AND**
    a. ONE of the following:
        i. The patient is less than 12 years of age and BOTH of the following:
            1. If the patient is less than 5 years of age BOTH of the following:
                a. The patient weighs greater than or equal to 6 kg; **AND**
                b. The prescriber has determined the patient is able to provide the minimum number of cells; **AND**
            2. ONE of the following **[medical record documentation required]**:
                a. The patient has a history of at least 100 mL/kg/year of packed red blood cells (pRBC) in the previous 12 months; **OR**
                b. The patient has required greater than or equal to 8 pRBC transfusions in the past 12 months; **OR**
        ii. The patient is at least 12 years of age but less than or equal to 50 years of age; **AND**
            1. ONE of the following **[medical record documentation required]**:
                a. The patient has a history of at least 100 mL/kg/year of pRBC in the past 12 months; **OR**
                b. The patient has required greater than or equal to 8 pRBC transfusions in the past 12 months; **AND**
2. The patient is clinically stable and able to undergo a hematopoietic stem cell transplant (HSCT) **[medical record documentation required]**; **AND**
3. The patient is a candidate for an allogeneic hematopoietic cell transplantation but has NO available willing and healthy 10/10 human leukocyte antigen (HLA)-matched related hematopoietic-cell donor **[medical record documentation required]**; **AND**
4. The patient does NOT have a white blood cell count < $3x10^9$/L and/or a platelet count <$100x10^9$/L **[medical record documentation required]**; **AND**

5. The patient does NOT have evidence of an uncorrected bleeding disorder **[medical record documentation required]**; **AND**
6. ONE of the following:
    a. The patient does NOT have any prior or current malignancy that required systemic therapy **[medical record documentation required]**; **OR**
    b. The patient had adequately treated cone-biopsied in situ carcinoma of the cervix uteri **[medical record documentation required]**; **OR**
    c. The patient had adequately treated basal or squamous cell carcinoma of the skin **[medical record documentation required]**; **AND**
7. The patient does NOT have advanced liver dysfunction as defined by any of the following **[medical record documentation required]**:
    a. Alanine transaminase (ALT) 3 times the upper limit of normal; **OR**
    b. Bilirubin above 3 times the upper limit of normal; **OR**
    c. Alkaline phosphatase above 3 times the upper limit of normal; **OR**
    d. International normalized ratio (INR) greater than or equal to 1.4; **AND**
8. The patient does NOT have a cardiac T2* result of <10ms by magnetic resonance imaging (MRI) **[medical record documentation required]**; **AND**
9. The patient does NOT have severe iron overload that in the provider's opinion warrants exclusion **[medical record documentation required]**; **AND**
10. The patient is NOT HIV positive **[medical record documentation required]**; **AND**
11. ONE of the following:
    a. The patient has a negative hepatitis B surface antigen (HBsAg) AND negative hepatitis B core antibody (HBcAB) **[medical record documentation required]**; **OR**
    b. The patient's HBcAB is positive due to a resolved hepatitis B infection AND the patient's HBV virus DNA is negative **[medical record documentation required]**; **AND**
12. ONE of the following:
    a. The patient's hepatitis C virus (HCV) antibody is negative **[medical record documentation required]**; **OR**
    b. The patient's HCV antibody is positive AND the patient's HCV RNA is negative **[medical record documentation required]**; **AND**
13. The patient does NOT have another active infection **[medical record documentation required]**; **AND**
14. The patient will receive granulocyte-colony stimulating factor (G-CSF) and plerixafor to mobilize stem cells prior to apheresis; **AND**
15. The patient will receive full myeloablative conditioning with busulfan; **AND**
16. The patient has NOT had previous gene therapy for the requested diagnosis **[medical record documentation required]; AND**
17. The patient will discontinue any disease-modifying therapies for β-thalassemia major or TDT (e.g., mitapivat) prior to the planned start of hematopoietic stem cell (HSC) mobilization and myeloablative conditioning **[medical record documentation required]**; **AND**
18. The requested dose is within FDA labeled dosing for the requested indication **[medical record documentation required]**.

Duration of Approval: 365 days (1 year); one-time, single-course treatment per lifetime

Please note, for certain identified gene and cellular therapies such as betibeglogene autotemcel (Zynteglo®), when coverage is available and the individual meets medically necessary criteria, distribution from a specialty pharmacy provider due to cost (distribution channel restriction) may be required in order for coverage to be provided. **Please contact Blue Cross NC to coordinate this therapy.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
betibeglogene autotemcel (Zynteglo®) intravenous (IV) infusion	Stem cell-based gene therapy to treat adult and pediatric patients who have transfusion-dependent beta-thalassemia	Single dose for infusion containing a suspension of CD34+ cells	J3393	1

***Maximum units allowed for duration of approval**

Other revenue codes that may be applicable to this policy: 0891, 0892

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

April 2026: Coding change: Added the following applicable revenue codes associated with policy HCPCS code(s): 0891 (Special Processed Drugs – FDA Approved Cell Therapy) and 0892 (Special Processed Drugs – FDA Approved Gene Therapy). **Policy notification given 2/1/2026 for effective date 4/1/2026**.
January 2026: Criteria change: For TDT indication: Added a requirement to discontinue any disease-modifying therapies for TDT (e.g., mitapivat) prior to initiating treatment, due to the recent FDA approval of a new therapy for TDT.
July 2024: Coding change: Added HCPCS code J3393 to dosing reference table effective 7/1/2024; deleted C9399, J3490, and J3590 termed 6/30/2024.
July 2024: Criteria change: Added criteria that patient has no available willing and healthy 10/10 human leukocyte antigen (HLA)-matched related hematopoietic-cell donor. **Policy notification given 5/1/2024 for effective date 7/1/2024**.

January 2023: Criteria update: Adjusted duration of approval for one-time, single-course treatment per lifetime to 365 days (1 year).
January 2023: Criteria update: Added distribution channel restriction language to policy. Adjusted formatting and defined authorization length for clarity with no change to policy intent. **Policy notification given 11/1/2022 for effective date 1/1/2023**.
August 2022: Original medical policy criteria issued.