

Zynteglo (betibeglogene autotemcel)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Zynteglo (betibeglogene autotemcel) is FDA-approved for the treatment of adult and pediatric patients with β -thalassemia who require regular red blood cell (RBC) transfusions. It works by helping the body make healthy red blood cells, thereby reducing the need for blood transfusions.

Thalassemia is a blood disorder that causes anemia (a low level of red blood cells) due to one or more genes that make hemoglobin not working like it should. It is normally inherited, passed down through gene mutations (abnormal gene changes) from parent to child. Thalassemia can be one of two types, alpha or beta, depending on which genes are affected.

Depending on which genes are involved and how severely they are affected, β -thalassemia can be:

- Mild - such as those with beta beta thalassemia trait (but don't have symptoms)
- A less severe form - such as non-transfusion-dependent beta thalassemia. Blood transfusions may be needed in certain cases, but not often.

- Severe - such as transfusion-dependent beta thalassemia. Blood transfusions are required, usually starting in childhood. The most severe of patients need at least 100 mL/kg/year of packed red blood cells (pRBCs) or ≥8 transfusions per year, and produce little to no β -globin.

Treatment varies depending on the type and severity of the condition. It may include:

- Blood transfusions
- Folic acid (vitamin B) supplements
- Calcium and vitamin D supplements
- Drugs to help remove iron buildup (chelation), which happens due to blood transfusions
- Removal of the spleen, if it becomes damaged
- Stem cell or bone marrow transplant, if transfusions are not working
- Novel therapies such as Reblozyl (luspatercept) or Zynteglo (betibeglogene autotemcel)

Definitions

“**Anemia**” is a condition in which there is a low level of red blood cells.

“Blood transfusion” is when a person gets blood that was given (donated) by another person.

“**Bone marrow transplant**” also known as “**stem cell transplant**” is a procedure that involves getting bone marrow cells from a donor (usually a sibling with similar genes, without or with a milder form of the condition/mutation).

“**Hemoglobin**” is a protein in red blood cells that carry oxygen from the lungs to the rest of the body.

Medical Necessity Criteria for Authorization

The Plan considers Zynteglo (betibeglogene autotemcel) medically necessary when **ALL** of the following criteria are met:

1. Prescribed by or in consultation with a hematologist; **AND**
2. The member is 4 years of age or older; **AND**
3. The member has a confirmed diagnosis β -thalassemia major AND a history of ONE of the following in the previous 2 years:
 - a. Transfusion of at least 100 mL/kg of body weight of packed red blood cells (pRBCs) per year; **or**

- b. Eight or more (≥ 8) transfusions of pRBCs per year; **AND**
4. The member is an appropriate candidate for hematopoietic stem cell transplantation (HSCT) but without a matched related (i.e., family) donor; **AND**
5. The member does NOT have ANY of the following:
 - a. A known and available human leukocyte antigen (HLA) matched family donor; **or**
 - b. Active bacterial, viral, fungal, or parasitic infection; **or**
 - c. Advanced liver disease, defined as:
 - i. Baseline alanine transaminase or direct bilirubin value $>3 \times$ the upper limit of normal (ULN); **or**
 - ii. Liver biopsy demonstrating cirrhosis, any evidence of bridging fibrosis, or active hepatitis; **or**
 - d. Any prior or current malignancy or myeloproliferative or immunodeficiency disorder; **or**
 - e. Contraindications to the conditioning regimen; **or**
 - f. Evidence of severe iron overload; **or**
 - g. Is pregnant or breast-feeding; **or**
 - h. Positive for presence of human immunodeficiency virus type 1 or 2 (HIV-1, HIV-2), hepatitis B virus (HBV), or hepatitis C (HCV); **or**
 - i. Prior treatment with HSCT or Zynteglo (betibeglogene autotemcel); **or**
 - j. Renal impairment, defined as creatinine clearance ≤ 70 mL/min/1.73 m²; **AND**
6. Dose is within the recommended range of:
 - a. Minimum of 5.0×10^6 CD34+ cells/kg; **and**
 - b. Maximum of 42.1×10^6 CD34+ cells/kg.

Experimental or Investigational / Not Medically Necessary

Zynteglo (betibeglogene autotemcel) for any other indication is *not covered* by the Plan, as it is considered experimental or investigational. Non-covered indications include, but are not limited to, the following:

- For the treatment of severe sickle cell disease (SCD).
- Re-treatment [Zynteglo (betibeglogene autotemcel) is indicated for one-time single-dose intravenous use only].

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics
ICD-10 codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
D56.1	Beta thalassemia
D56.2	Delta-beta thalassemia
D56.5	Hemoglobin E-beta thalassemia
ICD-10 codes <i>not</i> considered medically necessary:	
<i>Code</i>	<i>Description</i>
D50.0	Iron deficiency anemia secondary to blood loss (chronic)
D50.1	Sideropenic dysphagia
D50.8	Other iron deficiency anemias
D50.9	Iron deficiency anemia, unspecified
D55.21	Anemia due to pyruvate kinase deficiency
D55.29	Anemia due to other disorders of glycolytic enzymes
D59.10	Autoimmune hemolytic anemia, unspecified
D59.11	Warm autoimmune hemolytic anemia
D59.12	Cold autoimmune hemolytic anemia
D59.13	Mixed type autoimmune hemolytic anemia
D59.19	Other autoimmune hemolytic anemia
D57.00	Hb-SS disease with crisis, unspecified

D57.01	Hb-SS disease with acute chest syndrome
D57.02	Hb-SS disease with splenic sequestration
D57.03	Hb-SS disease with cerebral vascular involvement
D57.09	Hb-SS disease with crisis with other specified complication
D57.1	Sickle-cell disease without crisis
D57.20	Sickle-cell/Hb-C disease without crisis
D57.211	Sickle-cell/Hb-C disease with acute chest syndrome
D57.212	Sickle-cell/Hb-C disease with splenic sequestration
D57.219	Sickle-cell/Hb-C disease with crisis, unspecified
D57.80	Other sickle-cell disorders without crisis
D57.811	Other sickle-cell disorders with acute chest syndrome
D57.812	Other sickle-cell disorders with splenic sequestration
D57.819	Other sickle-cell disorders with crisis, unspecified
D63.0	Anemia in neoplastic disease
D63.1	Anemia in chronic kidney disease
D63.8	Anemia in other chronic diseases classified elsewhere
D64.81	Anemia due to antineoplastic chemotherapy

CPT/HCPCS Codes covered but may be subject to medical-necessity review:	
<i>Code</i>	<i>Description</i>
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)

References

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4. Lal A, Wong T, Keel S, et al. The transfusion management of beta thalassemia in the United States. *Transfusion*. 2021;61(10):3027-3039. doi:10.1111/trf.16640
5. 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
6. Magrin E, Semeraro M, Hebert N, et al. Long-term outcomes of lentiviral gene therapy for the β -hemoglobinopathies: the HGB-205 trial. *Nat Med*. 2022;28(1):81-88. doi:10.1038/s41591-021-01650-w
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Clinical Guideline Revision / History Information

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