Oscar Clinical Guideline: Zynteglo (betibeglogene autotemcel) (CG073, Ver. 4)

# Zynteglo (betibeglogene autotemcel)



## Summary

Beta thalassemia is an inherited blood disorder caused by mutations in the beta-globin gene, leading to reduced or absent beta-globin production. In transfusion-dependent beta thalassemia, the severe imbalance in alpha- and beta-globin chains results in ineffective erythropoiesis (creation of red blood cells), severe anemia, and complications from iron overload due to chronic transfusions. Standard treatment is regular red blood cell transfusions and iron chelation therapy. Allogeneic hematopoietic stem cell transplant can be curative but is limited by donor availability and transplant-related risks.

Zynteglo (betibeglogene autotemcel) is FDA-approved for the treatment of adult and pediatric individuals with beta 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.

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 (1) 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 meets ALL of the following criteria:
    a. No evidence of a known and available human leukocyte antigen (HLA) matched family donor*; and*
    b. No evidence of active bacterial, viral, fungal, or parasitic infection*; and*
    c. No evidence of advanced liver disease, defined as:
        i. Baseline alanine aminotransferase, aspartate aminotransferase or direct bilirubin value greater than (>)3 times the upper limit of normal (ULN)*; or*
        ii. Liver biopsy demonstrating cirrhosis, any evidence of bridging fibrosis, or active hepatitis*; or*
    d. No evidence of any prior or current malignancy or myeloproliferative or significant immunodeficiency disorder*; and*
    e. No evidence of contraindications to the conditioning regimen*; and*
    f. No evidence of severe iron overload*; and*

g. No evidence of pregnancy or breast-feeding*; and*
h. No evidence of presence of human immunodeficiency virus type 1 or 2 (HIV-1, HIV-2), hepatitis B virus (HBV), or hepatitis C (HCV)*; and*
i. No evidence of prior treatment with HSCT or Zynteglo (betibeglogene autotemcel)*; and*
j. No evidence of renal impairment, defined as creatinine clearance ≤ 70 mL/min/1.73 $m^2$*; 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 x $10^6$ CD34+ cells/kg.

<u>If the above criteria are met, Zynteglo (betibeglogene autotemcel) will be authorized for one dose per lifetime, with an approval duration of 18 months.</u>

### 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). There is no high-quality evidence to support the safety and efficacy of Zynteglo (betibeglogene autotemcel) for the management of sickle cell disease.
- 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: | |
| *Code* | *Description* |
| 96365 | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour |
| J3393 | Injection, betibeglogene autotemcel, per treatment |
| ICD-10 codes considered medically necessary if criteria are met: | |
| *Code* | *Description* |
| D56.1 | Beta thalassemia |
| D56.2 | Delta-beta thalassemia |
| D56.5 | Hemoglobin E-beta thalassemia |

| ICD-10 codes *not* considered medically necessary: | |
|---|---|
| *Code* | *Description* |
| 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: |
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| *Code* | *Description* |
|---|---|
| 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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## Clinical Guideline Revision / History Information

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