Inland Empire Health Plan

Drug Class Prior Authorization Criteria
betibeglogene autotemcel (Zynteglo)

Line of Business: Medi-Cal
P & T Approval Date: May 3, 2024 **Effective Date:** June 1, 2024

These criteria have been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the IEHP Pharmacy and Therapeutics Subcommittee.

Prior Authorization criteria is available for:

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Covered Uses: Zynteglo 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) transfusions.

Exclusion Criteria:

1. Received prior allogeneic hematopoietic stem cell transplant (HSCT)
2. Received prior gene therapy
3. Advanced liver disease defined as one of the following:
    a. Alanine transferases or direct bilirubin greater than 3 times the upper limit of normal (ULN)
    b. Baseline prothrombin time or partial thromboplastin time greater than 1.5 times the ULN suspected of arising from liver disease
    c. Magnetic resonance imaging (MRI) of the liver demonstrating clear evidence of cirrhosis
    d. Any evidence of bridging fibrosis, or active hepatitis
4. Positive for the presence of HIV type 1 or 2. Apheresis material from patients with a positive test for HIV will not be accepted for Zynteglo manufacturing.
5. Prior malignancy or has current malignancy (with the exception of adequately treated cone biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin) or myeloproliferative or significant immunodeficiency disorder.
6. Severely elevated iron in the heart (i.e., patients with cardiac T2* less than 10 msec by magnetic resonance imaging [MRI]) in the opinion of treating physician. Patients who had severely elevated iron in the heart (i.e., patients with cardiac T2* less than 10 msec by magnetic resonance imaging [MRI]) or advanced liver disease were not accepted into the studies.
7. White blood cell count less than 3 X 10^9 /L, and/or platelet count less than 100 X 10^9/L not related to hypersplenism.
8. Member has renal impairment, defined as creatinine clearance $\leqslant$ 70 mL/min/1.73 m2
9. Not to be administered to women who are pregnant.

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Required Medical Information:

1. Diagnosis of β-thalassemia with genetic confirmation (e.g., β0/β+, βE/β0, β+/β+, β0/β+ (IVS-I-110) and β+ (IVS-I-110)/β+ (IVS-I-110).
2. Member meets one of the following (a or b or c):
    a. Age ≥ 4 year-old and ≤ 12 year-old:
        i. Weight ≥ 6 kg;
        ii. Provider submits medical rationale that member is anticipated to be able to provide at least the minimum number of cells required to initiate the manufacturing process
    b. Age > 12 year-old and ≤ 17 year-old:
        i. Documentation with a β+ genotype, AND,
        ii. who do not have an HLA-compatible sibling donor
    c. Age > 17 year-old and ≤ 55 year-old:
        i. Documentation with a β+ genotype, AND,
        ii. at risk or ineligible to undergo an allogenic HSC transplant but can otherwise undergo an autologous gene therapy procedure with an acceptable risk.
3. Screening for hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotropic virus 1 & 2 (HTLV-1/HTLV-2), and human immunodeficiency virus 1 & 2 (HIV-1/HIV-2) in accordance with clinical guidelines before collection of cells for manufacturing.
4. Documentation of one of the following (a or b):
    a. Receipt of ≥ 100 mL/kg packed red blood cells (pRBC) per year for the previous two years;
    b. For age ≥ 12 years: Receipt of ≥ 8 transfusions of pRBC per year for the previous two years;
5. Member is clinically stable and eligible to undergo myeloablative conditioning and HSCT (i.e. Documentation of Karnofsky performance score ≥ 80, or equivalent)
6. Dose contains a minimum of 5 x 10^6 CD34+ cells/kg.

Approval duration: One time infusion per lifetime

Age Restrictions: 4 years to 55 years

Prescriber Restrictions: Hematologist or Transplant specialist

Other Criteria:

- Do not take anti-retroviral medications or hydroxyurea for one month prior to mobilization, or for the expected duration for elimination of the medications, and until all cycles of apheresis are completed.
- Discontinue iron chelators 7 days prior to initiation of myeloablative conditioning. Avoid use of myelosuppressive iron chelators for 6 months after Zynteglo infusion.
- Zynteglo has not been studied
    - In children less than 4 years of age
    - In patients > 65 years of age

- In patients with hepatic impairment
- In patients with renal impairment

REFERENCES:

1. Thalassaemia International Federation. 2021 Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT). https://thalassaemia.org.cy/publications/tif-publications/guidelines-for-the-management-of-transfusion-dependent-thalassaemia-4th-edition-2021-v2/ Accessed April 8, 2024.
2. ZYNTEGLO (betibeglogene autotemcel suspension) [package insert]. Somerville, MA: bluebird bio, Inc.; November 2023.

Change Control		
Date	Change	RPH
01/09/2023	• New PA Criteria	RG
04/08/2024	• Updated **Exclusion Criteria, Required Medical Information,** and **Age Restrictions** • Created References.	SV