Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the
Blue Cross Blue Shield Association

Title: Zynteglo

Professional / Institutional
Original Effective Date: November 15, 2022
Latest Review Date: March 26, 2026
Current Effective Date: March 26, 2026

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

Indication	Dose
Beta Thalassemia	Zyntelgo is provided as a single dose for intravenous infusion containing a suspension of CD34+ cells in one or more infusion bags to achieve the patient-specific dose. The minimum recommended dose of Zynteglo is 5.0×10^6 CD34+ cells/kg

- Granulocyte-colony stimulating factor (G-CSF) and plerixafor should be used for mobilization and busulfan should be used for myeloablative conditioning.
- Myeloablative conditioning (e.g., busulfan) should not occur until Zyntelgo is received and stored at the treatment center and availability of the back-up cell collection is confirmed.
- Prophylaxis for hepatic veno-occlusive disease (VOD) is recommended prior to initiating myeloablative conditioning.
- After completion of the myeloablative conditioning, allow a minimum of 48 hours of washout before Zynteglo infusion.
- Zyntelgo is for autologous use only. Before infusion, confirm that the patient's identity matches the unique patient identifiers on the Zynteglo infusion bag(s). Do not infuse if the information on the patient-specific label does not match the intended patient.

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

I. Length of Authorization [1]

- Coverage will be provided for one treatment course (1 dose of Zynteglo) and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- A single dose of Zynteglo containing a minimum of 5.0×10^6 CD34+ cells/kg of body weight, in one or more infusion bags

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1 billable unit (1 treatment)

III. Initial Approval Criteria [1]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

- Patient is at least 4 years of age; **AND**
- Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative conditioning; **AND**
- Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2), and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**

- Patient does not have a history of hypersensitivity to dimethyl sulfoxide (DMSO); **AND**
- Patient has not used prophylactic HIV anti-retroviral medication or hydroxyurea within 30 days prior to mobilization *(or for the expected duration for elimination of those medications)* and until all cycles of apheresis are completed (Note: if a patient requires anti-retrovirals for HIV prophylaxis, confirm a negative test for HIV before beginning mobilization and apheresis); **AND**
- Iron chelation therapy has been discontinued for at least 7 days prior to initiating myeloablative conditioning therapy and myelosuppressive iron chelators will be avoided for 6 months post-treatment; **AND**
- Patient has not received other gene therapies [e.g.,Casgevy™ (exagamglogene autotemcel), etc.]**; **AND**
- Patient will receive periodic life-long monitoring for hematological malignancies; **AND**
- Patient is eligible to undergo hematopoietic stem cell transplant (HSCT) and has not had prior HSCT; **AND**
- Patient does not have a known and available human leukocyte antigen (HLA) matched family donor willing to participate in an allogeneic HSCT; **AND**

Beta Thalassemia † Φ [1,4-7]

- Patient has a documented diagnosis of beta thalassemia (excludes alpha-thalassemia and hemoglobin S/ß-thalassemia variants) as outlined by the following:
    - Patient diagnosis is confirmed by *HBB* sequence gene analysis showing biallelic pathogenic variants; **OR**
    - Patient has severe microcytic hypochromic anemia, absence of iron deficiency, anisopoikilocytosis with nucleated red blood cells on peripheral blood smear, and hemoglobin analysis that reveals decreased amounts or complete absence of hemoglobin A (HbA) and increased HbA_2 with or without increased amounts of hemoglobin F (HbF); **AND**
- Patient has transfusion-dependent disease defined as a history of transfusions of at least 100 mL/kg/year of packed red blood cells (pRBCs) or with 8 or more transfusions of pRBCs per year in the 2 years preceding therapy; **AND**
- Patient will be maintained at a Hb ≥ 11 g/dL for 30 days prior to mobilization and 30 days prior to myeloablative conditioning; **AND**
- Patient does not have any of the following:
    - 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 (i.e., persistent AST, ALT, or direct bilirubin value > 3 times the upper limit of normal (ULN), baseline prothrombin time or partial thromboplastin time > 1.5 times the ULN, MRI of the liver demonstrated cirrhosis, or liver biopsy demonstrated bridging fibrosis, active hepatitis, or cirrhosis); **OR**
- Patients with an MRI of the liver with results demonstrating liver iron content ≥ 15 mg/g (unless biopsy confirms absence of advanced disease)

** *Requests for subsequent use of betibeglogene after receipt of other gene therapies (e.g., exagamglogene, etc.) will be evaluated on a case-by-case basis*

† FDA Approved Indications; ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage cannot be renewed.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CLINICAL RATIONALE

See package insert for FDA preshttps://dailymed.nlm.nih.gov/dailymed/index.cfm

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

HCPCS Code(s):

- J3393 – Injection, betibeglogene autotemcel, per treatment; 1 billable unit = 1 treatment

NDC:

- Zynteglo up to 4 infusion bags, 20 mL/infusion bag, overwrap, and metal cassette: 73554-3111-xx

REVISIONS	
11-15-2022	Policy added to the bcbsks.com web site. Policy maintained by Prime Therapeutics LLC
03-26-2024	Policy reviewed with no updates made. Policy maintained by Prime Therapeutics LC
07-01-2024	Added new code J3393 (eff. 07-01-2024)
10-08-2024	Policy reviewed by Prime Therapeutics with non-clinical edits
Posted 02-25-2026 Effective 03-26-2026	Policy reviewed and maintained by Prime Therapeutics LLC
	Updated Title: ▪ Removed: (betibeglogene autotemcel) Medical Drug Criteria Program Summary
	Changed Prior Authorization Clinical Criteria Approval to Initial Approval Criteria: ▪ Added criteria point for consideration of seizure prophylaxis prior to myeloablative conditioning ▪ Added life-long monitoring for hematological malignancies ▪ Added criteria for diagnosis of Beta Thalassemia ▪ Defined transfusion-dependent disease ▪ Added Iron overload criteria ▪ Added Hb level criteria pre/post myeloablative conditioning
	Replaced Clinical Rationale wording with a link to the FDA package insert

REFERENCES

1. Zynteglo [package insert]. Somerville, MA; Bluebird bio, Inc: August 2022. Accessed March 2024.
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3. Galanello R and Origa R. Beta-thalassemia. *Orphanet J Rare Dis.* 2010 May 21;5:11. Available at: https://ojrd.biomedcentral.com/articles/10.1186/1750-1172-5-11. Accessed March 2024.
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7. 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 Jan;28(1):81-88. doi: 10.1038/s41591-021-01650-w. Epub 2022 Jan 24.
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