Clinical Policy: Betibeglogene Autotemcel (Zynteglo)

Reference Number: CP.PHAR.545
Effective Date: 11/2022
Last Review Date: 07/2023

Coding Implications
Revision Log

Description

Betibeglogene autotemcel (Zynteglo®) is an autologous hematopoietic stem cell-based gene therapy.

FDA Approved Indication(s)

Zynteglo is indicated for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell (RBC) transfusions.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Zynteglo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Only for initial treatment dose; subsequent doses will not be covered.*

A. β-Thalassemia (must meet all)**:**

1. Diagnosis of β-thalassemia with genetic confirmation (*see Appendix E*);
2. Prescribed by or in consultation with a hematologist and transplant specialist;
3. Member meets one of the following (a or b):
   a. Age ≥ 5 years and ≤ 50 years;
   b. If age < 5 years, member meets both of the following (i and ii):
      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;
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 (*see Appendix D*);
   b. For age ≥ 12 years: Receipt of ≥ 8 transfusions of pRBC per year for the previous two years (*see Appendix D*);
5. Attestation from transplant specialist for both of the following (a and b):
   a. Member understands the risks and benefits of alternative therapeutic options such as allogeneic hematopoietic stem cell transplantation (HSCT);
   b. Member is clinically stable and eligible to undergo myeloablative conditioning and HSCT;
6. Member has not received prior allogeneic HSCT or gene therapy;
7. Member does not have advanced liver disease (*see Appendix D*);

8. Member is not positive for the presence of HIV type 1 or 2;
9. Member does not have any prior or current malignancy;
10. Dose contains a minimum of 5 x 10^6 CD34+ cells/kg.

Approval duration: 3 months (one time infusion per lifetime)

B. Other diagnoses/indications (must meet 1 or 2):
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy PA.CP.PMN.16
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy*

A. β-Thalassemia
1. Re-authorization is not permitted.

Approval duration: Not applicable

B. Other diagnoses/indications
1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
Approval duration: Duration of request or 6 months (whichever is less); or
2. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy PA.CP.PMN.16
3. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HIV: human immunodeficiency virus
HSCT: hematopoietic stem cell transplantation
pRBC: packed red blood cells
RBC: red blood cell

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- None reported

Appendix D: General Information

- Conversion of RBC units from mL: 1 RBC unit in these criteria refers to a quantity of pRBC approximately 200-350 mL.
  - Sites who use transfusion bags within this range, or ≥ 350 mL, the conversion in units should be done by dividing the volume transfused to the patient by 350 mL.
  - Sites who use transfusion bags < 200 mL, the conversion in units should be done by dividing the volume transfused to the patient by 200 mL.
- Examples of advanced liver disease include, but are not limited to, the following:
  - Cirrhosis
  - Active hepatitis
  - Bridging fibrosis
  - Fatty liver disease

Appendix E: Genetic Confirmation of β-Thalassemia

Beta Thalassemia Genotype Examples
β^0/β^0
β^0/β^+
β^+/β^+
β^E/β^0
β^+ IVS1-110/β^+ IVS1-110
β^0 /β^+ IVS1-110

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
β-thalassemia	Minimum dose: 5×10^6 CD34+ cells/kg	No maximum dose

VI. Product Availability

Single-dose cell suspension: up to four infusion bags of transduced CD34+ cells in cryopreservation solution labeled for the specific recipient

VII. References

1. Zynteglo Prescribing Information. Somerville, MA: bluebird bio, Inc.; August 2022. Available at: https://www.bluebirdbio.com/-/media/bluebirdbio/CorporateCOM/Files/Zynteglo/ZYNTEGLO_Prescribing_Information.pdf. Accessed April 24, 2023.
2. ClinicalTrials.gov. A study evaluating the efficacy and safety of the Lentiglobin® BB305 drug product in subjects with transfusion-dependent β-thalassemia, who do not have a β0/β0 genotype. Last updated June 25, 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT02906202. Accessed June 26, 2021.
3. ClinicalTrials.gov. A study evaluating the efficacy and safety of the Lentiglobin® BB305 drug product in subjects with transfusion-dependent β-thalassemia. Last updated June 24, 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT03207009. Accessed June 26, 2021.
4. Locatelli F, Thompson AA, Kwiatkowski JL, et al. Betibeglogene autotemcel gene therapy for non-β0/β0 genotype β-thalassemia. N Engl J Med. 2022;386(5):415-427.

5. Porter JB, Thompson AA, Walters MC, et al. Improvement in erythropoiesis in patients with transfusion dependent β-thalassemia following treatment with betibeglogene autotemcel (LentiGlobin for β-thalassemia) in the phase 3 HGB-207 study. EHA 2020 Virtual Congress Abstract: S296.
6. Cappellini MD, Farmakis D, Porter J, et al. Guidelines for the management of transfusion dependent thalassemia (TDT) 4th Edition. Thalassemia International Federation (2021). Available at: https://thalassaemia.org.cy/publications/tif-publications/guidelines-for-the-management-of-transfusion-dependent-thalassaemia-4th-edition-2021/. Accessed May 3, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/2022	
3Q 2023 annual review: no significant changes; added additional TDT genotype examples to appendix E (β^+/β^+ and β^0/β^+ IVS1-110); references reviewed and updated.	07/2023	