Clinical Policy: Betibeglogene Autotemcel (Zynteglo)

Reference Number: PA.CP.PHAR.545
Effective Date: 11/2022
Last Review Date: 07/2025

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 Betibeglogene Autotemcel (Zynteglo) is **medically necessary** when the following criteria are met:

I. Requirements for Prior Authorization of Zynteglo (betibeglogene autotemcel)

A. Prescriptions That Require Prior Authorization

All prescriptions for Zynteglo (betibeglogene autotemcel) must be prior authorized.

B. Review of Documentation for Medical Necessity

In evaluating a request for prior authorization of a prescription for Zynteglo (betibeglogene autotemcel), the determination of whether the requested prescription is medically necessary will take into account whether the member:

1. Is prescribed Zynteglo (betibeglogene autotemcel) for an indication that is included in the U.S. Food and Drug Administration (FDA)-approved package labeling; AND
2. Is age-appropriate according to FDA-approved package labeling; AND
3. Is prescribed a dose and number of treatments that are consistent with FDA-approved package labeling; AND
4. Is prescribed Zynteglo (betibeglogene autotemcel) by a specialist at an authorized treatment center for Zynteglo (betibeglogene autotemcel); AND
5. Does not have a contraindication to the prescribed medication; AND
6. Is not a prior recipient of gene therapy or an allogeneic hematopoietic stem cell transplant; AND
7. For treatment of transfusion-dependent β-thalassemia, both of the following:
    i. Has genetic testing confirming diagnosis of β-thalassemia

ii. Has a history of at least 100 mL/kg/year or 8 transfusion episodes/year of packed red blood cell transfusions in the prior 2 years.

NOTE: If the member does not meet the clinical review guidelines above but, in the professional judgement of the physician reviewer, the services are medically necessary to meet the medical needs of the member, the request for prior authorization will be approved.

C. Clinical Review Process

Prior authorization personnel will review the request for prior authorization and apply the clinical guidelines in Section B. above to assess the medical necessity of a prescription for a Zynteglo (betibeglogene autotemcel). If the guidelines in Section B. are met, the reviewer will prior authorize the prescription. If the guidelines are not met, the prior authorization request will be referred to a physician reviewer for a medical necessity determination. Such a request for prior authorization will be approved when, in the professional judgment of the physician reviewer, the services are medically necessary to meet the medical needs of the member

D. Dose and Duration of Therapy

Requests for prior authorization of Zynteglo (betibeglogene autotemcel) will be approved for 18 months for 1 infusion.

I. 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

II. Dosage and Administration

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

III. Product Availability

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

IV. References

1. Zynteglo [prescribing information]. Somerville, MA: bluebird bio, Inc.; August 2022.
2. Cappellini MD, Farmakis D, Porter J, Taher A, eds. 2021 Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT). 4th ed. Thalassaemia International Federation (TIF). Available at: https://thalassaemia.org.cy/. Accessed March 2024.
3. Connor RF, Fosmarin AG, Tirnauer JS. What's new in hematology. UpToDate [internet database]. Waltham, MA: UpToDate Inc. Updated February 29, 2024. Accessed March 18, 2024.

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
J3393	Injection, betibeglogene autotemcel, per treatment

Reviews, Revisions, and Approvals	Date
Policy created	10/2022

Reviews, Revisions, and Approvals	Date
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
Updated to match DHS criteria, effective 07/15/2024.	07/2024
2Q 2025 annual review: Added HCPCS code [J3393] and removed HCPCS codes [J3590, C9399]	05/2025