MetroPlus Health

Policy and Procedure

Title: Zynteglo (betibeglogene autotemcel)	**Division: Medical Management** **Department: Utilization Management**
Approval Date: 11/25/24	**LOB: Medicaid, HIV SNP, HARP, CHP, MetroPlus Gold, Goldcare, QHP, EP, Medicare, Ultracare**
Effective Date: 11/25/24	**Policy Number: UM-MP350**
Review Date: 2/17/2026	**Cross Reference Number:**
Retired Date:	**Page 1 of 8**

1. **POLICY DESCRIPTION:**
   Rare Blood Disorders – Cellular Immunotherapy, Autologous; Gene therapy, Zynteglo (betibeglogene autotemcel)

2. **RESPONSIBLE PARTIES:**
   Medical Management Administration, Utilization Management, Integrated Care Management, Pharmacy, Claim Department, Providers Contracting.

3. **DEFINITIONS:**
   Zynteglo is a one-time gene therapy that is FDA approved for the treatment of adult and pediatric patients who require packed red blood cell (pRBC) transfusions for β-thalassemia major also known as Cooley's Anemia. This condition is caused by a mutation in the β-globin gene leading to reduced or complete absence of β-globin, which is a protein necessary for normal hemoglobin function.

   Zynteglo is made specific for each patient where the patient's own red blood stem cells (autologous CD34+ hematopoietic cells) are collected through a process called mobilization & aphersis using granulocyte colony-stimulating factor (G-CSF) and plerixafor. The stem cells are sent to a manufacturing site to create Zynteglo, which takes around 70-90 days to manufacture. The stem cells are introduced to a lentiviral vector called BB305 which contains functional copies of modified β-globin gene. The vector will enter the patient's stem cells and incorporate the functional genes. Zynteglo will then be tested and shipped to the facility where the patient will receive the infusion.

   The patient will be admitted and undergo myeloablative conditioning where chemotherapy is given via busulfan to make space in the bone marrow. Following a washout period of at least 48 hours, Zynteglo will be infused intravenously for a one-time dose and the newly modified stem cells will reach the bone marrow and begin differentiating into RBCs. These new RBCs contain modified β-globin protein ($\beta^{A\text{-}T87Q}$-globin) that combine with α-globin, which creates functional hemoglobin A (HbA^{T87Q}). The expression of β-globin protein will gradually correct the imbalance of β/α globin in erythroid cells, which will allow hemoglobin A and total hemoglobin levels to reach normal and provide the patient to be independent of RBC transfusions. Once the patient completes the infusion they are to remain in the hospital for 3-6 weeks for monitoring purposes.

4. POLICY:

The following coverage criteria must be met in order for Zynteglo to be considered medically necessary for the treatment of patients with β-thalassemia major.

INITIAL REQUEST:

For Medicaid, HARP, and SNP Plan members, medical necessity will be determined using the NYS Department of Health Zynteglo Clinical Criteria Worksheet. The Plan will follow the instructions outlined by NYRx. Zynteglo is reimbursed by the Medicaid fee-for-service pharmacy program.

For all other Plan members, see criteria below:

1. β-Thalassemia

A. Zynteglo will be prescribed by or through the consultation of a hematologist;

AND

B. Member is ≥ 4 years of age but ≤ 50 years of age;

AND

C. Member weighs ≥ 6 kg (current (within past 30 days) weight has been documented in clinical chart notes);

AND

D. Member has a confirmed diagnosis of transfusion-depended β-thalassemia major defined as ONE of the following:

i. Transfusion-depended β-thalassemia is defined as a history of at least 100 mL/kg/year of packed red blood cells (pRBC) in the two (2) years preceding administration of betibeglogene autotemcel;

OR

ii. Transfusion-depended β-thalassemia with greater than or equal to eight (8) transfusions of pRBCs per year in the two(2) years preceding administration of betibeglogene autotemcel;

AND

E. Member has ONE of the following genotypes confirmed by DNA analysis:

i. Non-β^0/β^0 genotypes;

OR

ii. β^0/β^0 genotypes;

AND

F. Member has not received prior hematopoietic stem cell transplant (HSCT);

AND

G. ALL of the following:

i. Member is a candidate to undergo hematopoietic stem cell transplantation (HSCT);

AND

ii. Member is ineligible for allogenic hematopoietic stem cell transplantation due to the absence of a suitable donor (fully matched donor OR matched sibling donor);

AND

H. Member has the minimum number of blood stem cells (5.0×10^6 CD34+ cells/kg);

AND

I. Member does not have ANY of the following conditions:

i. Positive for the presence of human immunodeficiency virus (HIV) type 1 or type 2, hepatitis B virus (HBV) or hepatitis C (HCV) *[Note: If a member requires anti-retrovirals for HIV prophylaxis, then a negative test for HIV must be confirmed before beginning mobilization and apheresis of CD34+ cells];*

OR

ii. Any prior or current malignancy;

OR

iii. Renal impairment defined as creatinine clearance less than or equal to70 mL/min/1.73 m2

OR

iv. Advanced liver disease (e.g., alanine transaminase or aspartate transaminase greater than three times upper limit of normal, direct bilirubin value greater than three times upper limit of normal, bridging fibrosis, cirrhosis, active hepatitis);

OR

v. Severely elevated iron in the heart (i.e., patients with cardiac T2* less than 10 msec by MRI);

OR

vi. Current active infection;

AND

J. ONE of the following:

i. If member is biologically female of childbearing age, member meets ALL of the following:

1. Member has a negative serum pregnancy test before mobilization and re-confirmed prior to conditioning and right before administration of Zynteglo;

AND

2. Member will use an effective method of contraception from the start of mobilization through at least 6 month after Zynteglo administration;

OR

ii. If member is biologically male, member will use an effective method of contraception from the start of mobilization through at least 6 month after Zynteglo administration;

AND

K. Member will discontinue iron chelators at least seven days prior to initiation of myeloablative conditioning;

AND

L. Member has not received any previous treatment with Zynteglo or any other gene therapy, and is not being considered for other gene therapy, or investigational cellular therapy for β-Thalassemia;

AND

M. Member is not currently enrolled in a β-Thalassemia clinical trial or is ineligible for clinical trial enrollment

Initial Duration of Approval: *One time infusion per lifetime*

RENEWAL REQUEST:
Zynteglo will not be renewed for additional requests as this is a one-time therapy.

Renewal Duration of Approval: *Not Applicable*

5. LIMITATIONS/ EXCLUSIONS:

- Repeat infusions of Zynteglo are considered to be experimental and investigational because there have been no established studies to demonstrate effectiveness.
- Zynteglo is considered to be experimental and investigational if prescribed for indications other than for the treatment of β-thalassemia major in adult and pediatric populations.
- Zynteglo is only available at Qualified Treatment Centers.

6. APPLICABLE PROCEDURE CODES:

CPT	Description
J3393	Injection, betibeglogene autotemcel, per treatmentInjection, betibeglogene autotemcel, per treatment

7. APPLICABLE DIAGNOSIS CODES:

CODE	Description
D56.1	Beta thalassemia

8. REFERENCES:

1. Zynteglo (betibeglogene autotemcel) [Package Insert]. Somerville, MA: BlueBird Bio Inc. August 2022.
2. Locatelli F, Thompson AA, Kwiatkowski JL, et al. Betibeglogene Autotemcel Gene Therapy for Non-β^0/β^0 Genotype β-Thalassemia. *N Engl J Med*. 2022;386(5):415-427. doi:10.1056/NEJMoa2113206
3. Clinicaltrials.gov. 2022. A Study Evaluating the Efficacy and Safety of the LentiGlobin® BB305 Drug Product in Participants With Transfusion-Dependent β-Thalassemia - Full Text View - ClinicalTrials.gov. [online] Available at: <https://www.clinicaltrials.gov/ct2/show/NCT03207009> [Accessed 13 October 2022].
4. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value Final Evidence Report Prepared For.; 2022. https://icer.org/wp-content/uploads/2021/11/ICER_Beta-Thalassemia_Final-Report_071922.pdf
5. Origa R. Beta-Thalassemia. In: Adam MP, Everman DB, Mirzaa GM, et al., eds. GeneReviews®. Seattle (WA): University of Washington, Seattle; September 28, 2000.
6. New York State Medicaid Update - January 2024 Volume 40 - Number 1. health.ny.gov.https://health.ny.gov/health_care/medicaid/program/update/2024/no01_2024-01.htm#Zynteglo

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REVISION LOG:

REVISIONS	INITIAL	DATE
Creation date	AKC	11/25/24
Annual Review	JL	2/17/2026

David Ackman Digitally signed by David Ackman Date: 2026.04.16 07:21:40 -04'00'

Approved:
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Sanjiv Shah MD Digitally signed by Sanjiv Shah MD Date: 2026.04.17 09:42:56 -04'00'

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Medical Guideline Disclaimer:

 The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, Metroplus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered andor paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members.

All coding and website links are accurate at time of publication.

MetroPlus Health Plan has adopted the herein policy in providing management, administrative and other services to our members, related to health benefit plans offered by our organization.