MetroPlus Health

Policy and Procedure

Title: Lyfgenia (lovotibeglogene autotemcel)	Division: Medical Management Department: Pharmacy
Approval Date: 11/25/2024	LOB: Medicaid, SNP, HARP, CHP, QHP, EP, Gold, Goldcare, Medicare, Ultracare
Effective Date: 11/25/2024	Policy Number: UM-MP349
Review Date: 6/16/2026	Cross Reference Number:
Retired Date:	Page 1 of 11

1. POLICY DESCRIPTION:

Hematological Agents; Hematopoietic Agents; Cellular Immunotherapy; Autologous; Gene Therapy - Lyfgenia (lovotibeglogene autotemcel)

2. RESPONSIBLE PARTIES:

Medical Management Administration, Pharmacy Department, Utilization Management, Integrated Care Management, Claims Department

3. DEFINITIONS:

Lyfgenia is an autologous hematopoietic stem cell-based gene therapy which adds functional copies of a modified βA-globin gene into patients' hematopoietic stem cells (HSCs) through transduction of autologous CD34+ cells with BB305 lentiviral vector (LVV).

After Lyfgenia infusion, the transduced CD34+ HSCs engraft in the bone marrow and differentiate to produce red blood cells containing biologically active βA-T87Q-globin that will combine with α-globin to produce functional Hb containing βA-T87Q-globin (HbAT87Q). HbAT87Q has similar oxygen-binding affinity and oxygen hemoglobin dissociation curve to wild-type HbA, reduces intracellular and total hemoglobin S (HbS) levels, and is designed to sterically inhibit polymerization of HbS thereby limiting the sickling of red blood cells.

Abbreviation	Description
SCD	Sickle Cell Disease
VOE	Vaso-Occlusive Event
HSCT	hematopoietic stem cell transplant
HLA	human leukocyte antigen
HIV	human immunodeficiency virus
HBV	hepatitis B
HCV	hepatitis C
ALT	alanine transaminase
INR	international normalized ratio
ACS	Acute chest syndrome
G-CSF	Granlocyte-colony stimulating factor

4. POLICY:

Lyfgenia will be considered medically necessary once the following coverage criteria is met. Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Chart notes must be submitted to confirm diagnosis and previous treatment(s).

INITIAL REQUEST:
For Medicaid, SNP, HARP Plan members, follow the criteria below. The Plan will follow the instructions outlined by NYRx and use the Cell and Gene Therapy Form to submit information to NYRx. Lyfgenia is reimbursed by the Medicaid fee-for-service pharmacy program.

1. **Sickle Cell Disease**
   a) Member is 12 years of age or older;
   AND
   b) Member has sickle cell disease (SCD);
   AND
   c) Member has a history of vaso-occlusive events (VOEs);
   AND
   d) Authorization is for one-time administration consistent with FDA labeling.

Additionally, New York State (NYS) Department of Health's memo released on 1/12/2026 requires NYS managed care plan should ensure:

- The gene therapy is administered at an in-network qualified treatment center or have a single case agreement.
- Providers who submit a claim must be a member of the CMS-designated patient registry (i.e., the Center for International Blood & Marrow Transplant Research - CIBMTR) and participate in a CMS-specified study. A list of participating centers is available on the CIBMTR website.
- Continuity of care for beneficiaries that may transition between fee-for-service and managed care, or among Managed Care Plans.
- Beneficiaries continue to have access to their Sickle Cell Disease gene therapy providers for at least one year after receiving gene therapy.
- Providers have access to a primary and secondary Managed Care Plan representative.
- A Managed Care Plan representative is aware of the coverage policy guidance in the October 2025 Medicaid Update.

For all non-Medicaid LoBs:
INITIAL REQUEST:
1. **Sickle Cell Disease (SCD) and a history of Vaso-Occlusive Events (VOEs)**

A. Member is ≥ 12 and ≤50 years of age;

AND

B. Member's current weight has been documented in clinical chart notes;

AND

C. Prescribed by or in consultation with a hematologist or a stem cell transplant physician;

AND

D. Member has a confirmed diagnosis with ONE of the following groups of SCD:

- **a.** βS/βS;

  OR

- **b.** βS/β0;

  OR

- **c.** βS/β+ genotype;

AND

E. Member has experienced four or more severe VOEs crises over the past 24 months as defined by ONE of the following:

- **a.** An episode of acute pain that resulted in a visit to a medical facility which required administration of at least ONE of the following:
  - **i.** Intravenous opioid;

    OR

  - **ii.** Intravenous nonsteroidal anti-inflammatory drug;

  OR

- **b.** Acute chest syndrome (i.e., presence of a new pulmonary infiltrate associated with pneumonia-like symptoms (e.g., chest pain, fever [> 38.5°C/101.3°F], tachypnea, wheezing or cough, or findings upon lung auscultation, presence of a new pulmonary infiltrate consistent with Acute chest syndrome (ACS) that requires oxygen treatment and/or blood transfusion);

  OR

- **c.** Acute hepatic sequestration (i.e., sudden increase in liver size associated with pain in the right upper quadrant, abnormal results of liver function test not due to biliary tract disease, and the reduction of hemoglobin concentration by ≥ 2 g/dL below the baseline value);

  OR

- **d.** Acute splenic sequestration (i.e., enlarged spleen, left upper quadrant pain, and an acute decrease in hemoglobin concentration of ≥ 2 g/dL below the baseline value);

OR

e. Acute priapism lasting > 2 hours and requiring a visit to a medical facility (i.e., sustained, unwanted painful erection lasting more than 2 hours and requiring care at a medical facility (with or without hospitalization)

AND

F. Member's Karnofsky performance status of ≥ 60 (≥16 years of age) or a Lansky performance status of ≥60 (<16 years of age);

AND

G. Member has adequate bone marrow function as confirmed by ONE of the following:

a. Absolute neutrophil count > 1,000/µL;

OR

b. Absolute neutrophil count > 500/µL for members taking hydroxyurea;

OR

c. Platelet count > 100,000/µL;

AND

H. Member has tried and failed ALL of the following for at least 6 months unless member has had a contraindication:

a. Hydroxyurea as monotherapy;

OR

b. Hydroxyurea in combination with other disease-modifying agents (e.g., Endari (L-glutamine), Adakveo (crizanlizumab));

AND

I. Member has not received a prior hematopoietic stem cell transplant;

AND

J. ALL of the following:

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

AND

b. Member is ineligible for allogeneic hematopoietic stem cell transplantation due to the absence or unwillingness of a suitable donor*; [Note: member will be considered ineligible for Lyfgenia if member declines allogeneic hematopoietic stem cell transplantation]*

AND

c. Member is ineligible for allogeneic hematopoietic stem cell transplantation due to the absence or unwillingness of a fully matched sibling donor; *[Note: member will be considered ineligible for Lyfgenia if member declines allogeneic hematopoietic stem cell transplantation]*

AND

K. Member does not have ANY of the following:

- **a.** More than two α-globin gene deletions;

OR

- **b.** Active infections (e.g., human immunodeficiency virus (HIV), hepatitis B (HBV), hepatitis C (HCV), Human T-lymphotrophic virus-1 and -2, bacterial, viral, fungal, parasitic infection);

OR

- **c.** Active liver disease (i.e. alanine transaminase (ALT) > 3 times upper limit of normal; direct bilirubin value > 2.5 times upper limit of normal; baseline prothrombin time (international normalized ratio [INR]) > 1.5 times upper limit of normal; cirrhosis; bridging fibrosis; or active hepatitis);

OR

- **d.** Contraindications to any product or procedure required for treatment (i.e., red blood cell transfusions, use plerixafor and busulfan);

OR

- **e.** History of severe cerebral vasculopathy, prior or current malignancy or immunodeficiency disorder, allogeneic transplant, considered for other HSCT and other gene therapy for SCD;

AND

L. Per provider, ALL of the following medications will be discontinued for the duration specified prior to mobilization if member is currently on them:

- **a.** Disease-modifying therapies for sickle cell disease for at least 2 months prior to mobilization and 2 days prior to conditioning (e.g., hydroxyurea, Endari (L-glutamine), Adakveo (crizanlizumab));

AND

- **b.** Erythropoietin for at least 2 months prior to mobilization;

AND

- **c.** Iron chelation therapy for at least 7 days prior to mobilization and 2 days prior to conditioning (e.g., deferoxamine injection, deferiprone tablets or solution, and deferasirox tablet);

AND

- **d.** Granlocyte-colony stimulating factor (G-CSF) not to be administered prior to or with mobilization agents;

AND

- **e.** Anti-retrovirals for at least 1 month prior to mobilization and until all cycles of apheresis are completed *(Note: long-acting anti-retrovirals (e.g.*

Cabenuva, Sunlenca, Trogarzo, Edurant) may require a longer duration of discontinuation for elimination of medication);

AND

M. ONE of the following:

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

i. Member has a negative serum pregnancy test before mobilization cycle and re-confirmed prior to myeloablative conditioning and right before administration of Lyfgenia;

AND

ii. Member will use an effective method of contraception from the start of mobilization through at least 6 months after Lyfgenia administration;

OR

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

AND

N. Member has not received Lyfgenia or any other gene therapy previously;

AND

O. Member is not currently enrolled in a SCD clinical trial or is ineligible for clinical trial enrollment

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

RENEWAL REQUEST:

Lyfgenia will not be renewed for additional requests as this is a one-time therapy.

Renewal Duration of Approval: *Not Applicable*

5. LIMITATIONS/ EXCLUSIONS:

Lyfgenia be considered experimental and investigational if prescribed for indications that have not been approved by the FDA and will not be covered under this policy.

Following treatment with Lyfgenia, members with α-thalassemia trait (-α3.7/-α3.7) may experience anemia with erythroid dysplasia that may require chronic red blood cell transfusions.

Lyfgenia is only available at Qualified Treatment Centers.

6. APPLICABLE PROCEDURE CODES:

CPT	Description
J3394	Injection, lovotibeglogene autotemcel, per treatment

7. APPLICABLE DIAGNOSIS CODES:

CODE	Description
D57.00	Hb-Ss Disease With Crisis, Unspecified
D57.01	Hb-Ss Disease With Acute Chest Syndrome
D57.02	Hb-Ss Disease With Splenic Sequestration
D57.03	Hb-Ss Disease With Cerebral Vascular Involvement
D57.04	Hb-Ss Disease With Dactylitis
D57.09	Hb-Ss Disease With Crisis With Other Specified Complication
D57.1	Sickle-Cell Disease Without Crisis
D57.20	Sickle-Cell/Hb-C Disease Without Crisis
D57.211	Sickle-Cell/Hb-C Disease With Acute Chest Syndrome
D57.212	Sickle-Cell/Hb-C Disease With Splenic Sequestration
D57.213	Sickle-Cell/Hb-C Disease With Cerebral Vascular Involvement
D57.214	Sickle-Cell/Hb-C Disease With Dactylitis
D57.218	Sickle-Cell/Hb-C Disease With Crisis With Other Specified Complication
D57.219	Sickle-Cell/Hb-C Disease With Crisis, Unspecified
D57.40	Sickle-Cell Thalassemia Without Crisis
D57.411	Sickle-Cell Thalassemia, Unspecified, With Acute Chest Syndrome
D57.412	Sickle-Cell Thalassemia, Unspecified, With Splenic Sequestration
D57.413	Sickle-Cell Thalassemia, Unspecified, With Cerebral Vascular Involvement
D57.414	Sickle-Cell Thalassemia, Unspecified, With Dactylitis
D57.418	Sickle-Cell Thalassemia, Unspecified, With Crisis With Other Specified Complication
D57.419	Sickle-Cell Thalassemia, Unspecified, With Crisis
D57.42	Sickle-Cell Thalassemia Beta Zero Without Crisis
D57.431	Sickle-Cell Thalassemia Beta Zero With Acute Chest Syndrome
D57.432	Sickle-Cell Thalassemia Beta Zero With Splenic Sequestration
D57.433	Sickle-Cell Thalassemia Beta Zero With Cerebral Vascular Involvement
D57.434	Sickle-Cell Thalassemia Beta Zero With Dactylitis
D57.438	Sickle-Cell Thalassemia Beta Zero With Crisis With Other Specified Complication

D57.439	Sickle-Cell Thalassemia Beta Zero With Crisis, Unspecified
D57.44	Sickle-Cell Thalassemia Beta Plus Without Crisis
D57.451	Sickle-Cell Thalassemia Beta Plus With Acute Chest Syndrome
D57.452	Sickle-Cell Thalassemia Beta Plus With Splenic Sequestration
D57.453	Sickle-Cell Thalassemia Beta Plus With Cerebral Vascular Involvement
D57.454	Sickle-Cell Thalassemia Beta Plus With Dactylitis
D57.458	Sickle-Cell Thalassemia Beta Plus With Crisis With Other Specified Complication
D57.459	Sickle-Cell Thalassemia Beta Plus With Crisis, Unspecified
D57.80	Other Sickle-Cell Disorders Without Crisis
D57.811	Other Sickle-Cell Disorders With Acute Chest Syndrome
D57.812	Other Sickle-Cell Disorders With Splenic Sequestration
D57.813	Other Sickle-Cell Disorders With Cerebral Vascular Involvement
D57.814	Other Sickle-Cell Disorders With Dactylitis
D57.818	Other Sickle-Cell Disorders With Crisis With Other Specified Complication
D57.819	Other Sickle-Cell Disorders With Crisis, Unspecified

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REVISION LOG:

REVISIONS	INITIAL	DATE
Creation date	AKC	11/25/24
Update	JL	6/16/2026

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Approved:
Sanjiv Shah, MD
Chief Medical Officer

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