Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines
Medical Benefit Drugs

Lyfgenia® (lovotibeglogene autotemcel)

Effective: January 1, 2026

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	Yes ☒ No ☐

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988
☒ Tufts Health Plan Commercial products; Fax 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988
☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans; Fax 617-673-0939
☐ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0939
☐ Tufts Health One Care-- A dual-eligible product; Fax 617-673-0956

Senior Products

☐ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956
☐ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956
☐ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Sickle cell disease (SCD) is a group of inherited debilitating blood disorders caused by a mutation in the β-globin gene that leads to the production of abnormal sickle shaped hemoglobin (HbS). In SCD, the sickled RBCs become rigid, undergo premature hemolysis leading to anemia, and become unable to transport oxygen to critical organs. The condition affects more than 100,000 people in the United States with an incidence of about 1 in every 365 Black births and 1 in every 16,300 Hispanic-American births.

Severely affected patients may experience diverse complications such as severe anemia, repeated acute painful vaso-occlusive events (VOEs) due to small-vessel obstruction (vaso-occlusive crises [VOCs]; sickle cell crises), acute chest syndrome (ACS; acute event with pneumonia-like symptoms), cerebral vasculopathy, chronic organ damage that may involve e.g., the bones, kidneys, heart, liver, and lungs or result in severe infectious complications such as functional hyposplenism and premature death. Treatment includes measures to control complications, relieve pain, prevent infections, and minimize organ damage. Standard pharmacologic treatment has included medications, such as hydroxyurea (Hydrea), analgesics and blood transfusions. Hematopoietic stem cell transplantation for patients with an appropriate donor, until the development of gene therapy, has been an option for cure. Gene therapies now offer a treatment option for members with severe sickle cell disease who do not have a willing HLA matched family donor.

Food and Drug Administration (FDA) Approved Indications:

- Lyfgenia is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events.

Lyfgenia uses an ex vivo lentiviral vector gene therapy which adds a functional copy of a modified βA-globin gene (threonine [T] into patients' HSCs through transduction of autologous CD34+ cells with BB305 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 inhibit polymerization of HbS thereby limiting the sickling of red blood cells.

NOTE: Lyfgenia can only be administered at a Lyfgenia Qualified Treatment Center (QTC). Each Lyfgenia QTC has been carefully selected based on their expertise in areas such as transplant, cell, and gene therapy. For information on locating a Qualified Treatment Center, please go to https://www.lyfgenia.com/find-a-qualified-treatment-center

Clinical Guideline Coverage Criteria

The Plan may cover Lyfgenia for sickle cell disease when **all** the following clinical criteria is met:

1. Member has a diagnosis of sickle cell disease with history of vaso-occlusive events (VOEs); **and**
2. Member is at least 12 years of age**; and**
3. Lyfgenia is prescribed by or in consultation a hematologist who specializes in the treatment of sickle cell disease**; and**
4. Member has documentation of recurrent vaso-occlusive crises (VOC) as defined by at least 4 vaso-occlusive events in the previous 2 years prior to screening for administration that required care at a medical facility. *Examples of VOCs include:
    a. Acute pain event requiring pain medication(s) or RBC transfusions
    b. Acute chest syndrome
    c. Priapism lasting >2 hours
    d. Acute splenic sequestration
    e. Acute hepatic sequestration
5. Member has tried and failed, has a contraindication, or intolerance to treatment with hydroxyurea or another disease modifying therapy (e.g., Adakveo (crizanlizumab), Endari (L-glutamine))**; and**
6. Member has not been previously treated with a gene therapy for sickle cell disease**; and**
7. Member has not been previously treated with any other gene therapies for any other disorder**; and**
8. Member is clinically stable and would be considered a candidate for allogenic hematopoietic stem cell transplantation (HSCT), but is ineligible due to the absence of a willing/acceptable HLA-matched family donor or any other condition(s) that the provider attests to which makes the member ineligible for HSCT**; and**
9. Member has not received prior treatment with any gene therapy or allogenic stem cell transplant for sickle cell disease; **and**
10. The prescriber attests that the Member has adequate organ function with no anticipated decline in organ function in close proximity to apheresis timeframe; **and**
11. The Member has no active infection (e.g., viral, bacterial, fungal, parasitic) including presence of HIV-1 and HIV-2, active hepatitis B or active hepatitis C. Screening must be completed at the time of apheresis; **and**
12. Lyfgenia will be administered at a Qualified Treatment Center

Note: *For Members who have been stabilized on continuous red blood cell transfusions because of stroke history or chronic SCD complications with history of recurrent VOCs may meet medical necessity with additional documentation provided.

Limitations

- Lyfgenia will not be covered if the Member demonstrates clinical decompensation from time of authorization to time of infusion and no longer meets clinical coverage criteria
- Any indications for Lyfgenia other than those outlined above are considered investigational and will not be covered
- Authorization of Lyfgenia is limited to one single dose treatment
- LYFGENIA will not be covered if the Member has more than one α-globin gene deletions (limitation of use for patients with α-thalassemia trait (-α3.7/-α3.7) and has not been studied in patients with more than two α-globin gene deletions)
- Members who have received prior gene therapy for sickle cell disease, including therapies in clinical trial settings, will not be approved for Lyfgenia

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J3394	Injection, lovotibeglogene autotemcel, per treatment

References:

1. A Study Evaluating the Safety and Efficacy of bb1111 in Severe Sickle Cell Disease; NCT02140554. Accessed at https://classic.clinicaltrials.gov/ct2/show/NCT02140554?term=NCT02140554&draw=2&rank=1 accessed February 1, 2024.
2. Lyfgenia (lovotibeglogene autotemcel). [package insert]. Somerville, MA: bluebird bio Inc; Dec 2023.
3. New Drug Review: Lyfgenia (lovotibeglogene autotemcel). IPD Analytics. January 2024.
4. Kanter J, et. al. Lovo-cel gene therapy for sickle cell disease: Treatment process evolution and outcomes in the initial groups of the HGB-206 study. Am J Hematol. 2023 Jan;98(1):11-22. doi: 10.1002/ajh.26741. Epub 2022 Oct 10. PMID: 36161320; PMCID: PMC10092845.
5. Herring WL, et. al. Cost-Effectiveness of Lovotibeglogene Autotemcel (Lovo-Cel) Gene Therapy for Patients with Sickle Cell Disease and Recurrent Vaso-Occlusive Events in the United States. Pharmacoeconomics. 2024 Jun;42(6):693-714. doi: 10.1007/s40273-024-01385-9. Epub 2024 Apr 29. PMID: 38684631; PMCID: PMC11126463.

Approval And Revision History

February 21, 2024: Reviewed by the Medical Policy Approval Committee (MPAC) effective April 1, 2024
Subsequent endorsement date(s) and changes made:

- May 15, 2024: Reviewed by MPAC, removed MATogether from MNG, MATogether will not use MassHealth criteria and administrative update per AMA HCPCS code J3394 added effective, July 1, 2024
- November 21, 2024: Reviewed by MPAC, updated criteria to remove Oxbryta as disease modifying therapy, added term “acceptable” to HLA matched family donor. Effective January 1, 2025.
- November 19, 2025: Reviewed by MPAC for annual review, renewed without changes, references updated, effective January 1, 2026
- December 2025: Administrative updates effective January 1, 2026.
- December 17, 2025: Reviewed by MPAC, RITogether remove as an applicable line of business, coverage moved to Gene Therapies for Sickle Cell Disease for RITogether effective January 1, 2026

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member’s benefit document, and in coordination with the Member’s physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.