Mass General Brigham
Health Plan

Lyfgenia
(lovotibeglogene autotemcel)

Policy Number: 078

	Commercial and Qualified Health Plans	MassHealth	Medicare Advantage
Authorization Required	X	X	X
No Prior Authorization			

Lyfgenia (lovotibeglogene autotemcel) is an autologous hematopoietic stem cell-based gene therapy for sickle-cell disease (SCD). In this therapy, autologous CD34+ hematopoietic stem cells are collected from the patient and then transfected with lovotibeglogene autotemcel. Once the cells are ready, the patient undergoes a conditioning regimen to replace their hematopoietic stem cells with the gene therapy stem cells. The gene therapy stem cells settle in the patient's bone marrow where they grow and produce new blood cells containing normally-functioning HBA^{T87Q}.

FDA-approved indications
For the treatment of patients aged 12 and older with SCD and a history of vaso-occlusive crises/episodes (VOC/VOE).

Coverage guidelines
Mass General Brigham Health Plan covers Lyfgenia when all of the following have been met:

1. Member is ≥12 years of age; and
2. Genetic test confirms SCD; and
3. At least 4 VOC/VOE in the past 24 months, including but not limited to:
    a. Acute pain event requiring a visit to a medical facility for pain medication(s) or red blood cell (RBC) transfusions;
    b. Acute chest syndrome;
    c. Acute splenic and/or hepatic sequestration;
    d. Priapism lasting longer than 2 hours and requiring a visit to a medical facility; and
4. Lab evaluation without evidence of advanced liver disease; and
5. No active/uncontrolled infections, including HIV, HBV, or HCV; and
6. One of the following:
    a. Inadequate response to treatment with hydroxyurea for at least 3 months, with good adherence to therapy based on pharmacy claims or provider documentation, or
    b. Adverse reaction or contraindication to the use of hydroxyurea, or
    c. Chronic transfusion therapy without hydroxyurea for primary or secondary stroke prevention; and
7. Treatment will be administered in a qualified treatment facility.

Mass General Brigham Health Plan considers Lyfgenia to be experimental/investigation for all other indications.

Exclusions

1. History of allogenic HSCT
2. History of any gene therapy treatment
3. One or more α-globin gene deletions

Medicaid Variation
Prior authorization requests for Lyfgenia for Mass General Brigham ACO members should be submitted to the MassHealth Drug Utilization Review Program. Criteria for Lyfgenia are found in Table 45: Beta Thalassemia, Myelodysplastic Syndrome, and Sickle Cell Disease Agents.

Medicare Variation
Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and documentation included in the Medicare manuals are the basis for coverage determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for coverage determinations. **As of Mass General Brigham Health Plan's most recent policy review, CMS had no NCDs or LCDs for gene therapy treatments for Sickle Cell Disease.**

Codes

The following codes are included for informational purposes only; inclusion of a code does not constitute or imply coverage.

The list of codes applies to commercial and MassHealth plans only.

Authorized CPT/HCPCS Codes	Code Description
38206	Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous
J3394	Injection, lovotibeglogene autotemcel

Summary of Evidence
Lovotibeglogene autotemcel (Lyfgenia, lovo-cel) lentiviral gene therapy represents a significant advance in sickle cell disease (SCD) treatment. In the single-arm, open-label Phase 1/2 trial HGB-206, patients aged 12-50 with SCD and at least 4 severe VOEs in the previous 24 months were treated with lovo-cel (Kanter et al. 2022). Among 35 treated patients, mean total hemoglobin increased from 8.5 to 11g/dL and HbA^{T87Q} represented at least 40% of total hemoglobin. Complete remission of VOEs was observed in 100% of 25 evaluable patients after at least 6 months of follow-up. Stomatitis and leukopenias were common, but serious adverse effects were rare. In the same study, quality of life improved among patients with baseline scores below the population norm but were stable among those with baseline scores "better or near" the population norm (Walters et al. 2021). However, two patients in the initial cohort of HGB-206 developed acute myeloid leukemia (Goyal et al. 2022), prompting addition of a black-box warning to the FDA label due to the risk of hematologic malignancy. The phase 3 trial HGB-210 is ongoing; in an outcomes update that combines study participants in HGB-206 and HGB-210, complete resolution of VOE over at least 18 months of follow-up was observed in 88%.

The evidence to date shows Lyfgenia to be a promising therapy for patients with SCD and severe VOEs, albeit with some associated risk of hematologic malignancy. Evidence is still needed on long-term safety and efficacy of this agent, and on long-term outcomes of its major competitor Casgevy. Relative cost-effectiveness of these agents remains uncertain and depends on the accuracy of predicted improvements in survival and in quality of life (Herring et al. 2024). MGB Health Plan considers lovo-cel to be medically necessary for members with SCD who meet criteria based on the inclusion criteria in the pivotal HGB-206 trial.

Effective
April 2025: Annual review. Clarified Medicaid and Medicare variations. Code list updated. MassHealth variation updated to include new prior authorization process.
March 2025: Ad hoc review. Summary of evidence added. References updated.

August 2024: Code update, retroactive to 7/1/2024
July 2024: Effective date.

References

Goyal S, Tisdal J, Schmidt M, et al. Acute myeloid leukemia case after gene therapy for sickle cell disease. *NEJM* 2022; 386(2):138-147.

Herring WL, Gallagher ME, Shah N, 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;42(6):693-714.

Kanter J, Walters MC, Krishnamurti L, et al. Biologic and clinical efficacy of LentiGlobin for sickle cell disease. NEJM 2022;386:617-28.

Kwiatkowski JL, Thompson AA, Rasko JEJ, et al. Long-term clinical outcomes of lentiglobin gene therapy for transfusion-dependent β- thalassemia in the Northstar (HGB-204) study. Blood 2019;134(Suppl 1):4628.

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Walters MC, Tisdal JF, Mapara MY, et al. Sustained improvements in patient-reported quality of life up to 24 months post-treatment with LentiGlobin for sickle cell disease (bb1111) gene therapy. Blood 2021;138(Suppl 1):7-9.