# PROVIDER POLICIES & PROCEDURES

## LYFGENIA™ (lovotibeglogene autotemcel)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for gene therapy with Lyfgenia (lovotibeglogene autotemcel). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

*Sickle cell disease (SCD)* is a single-gene inherited blood disorder in which the sickle mutation is coinherited with a pathogenic variant at the other beta-globin allele that reduces or abolishes normal beta-globin production. There are several variants of SCD including sickle cell anemia (homozygous sickle mutation [Hb SS]), sickle-beta thalassemia, hemoglobin SC disease, and others. The key feature of all types of SCD is that the Hb S proportion is typically >50 percent, and Hb S is the predominant hemoglobin. The major clinical features are related to hemolytic anemia and vaso-occlusion, which can lead to acute and chronic pain and tissue ischemia or infarction.

**Lyfgenia** is a single dose hematopoietic stem cell-based autologous gene addition therapy indicated for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events. It is designed to add functional copies of a modified anti-sickling adult hemoglobin ($HbA^{T87Q}$) into patients' own hematopoietic stem cells. The $HbA^{T87Q}$ reduces intracellular and total HbS levels and is designed to sterically inhibit polymerization of HbS thereby limiting the sickling of red blood cells to potentially decrease or stop vaso-occlusive events.

### CLINICAL GUIDELINE

Coverage decisions for the use of Lyfgenia will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage decisions are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

Treatment with Lyfgenia will be considered medically necessary for individuals with *sickle cell disease* when ALL of the following criteria are met:

A. The individual is 12 years of age or older; **AND**
B. The individual has a diagnosis of sickle cell disease with one of the following genotypes confirmed by genetic testing:
    a. $\beta^S/\beta^S$
    b. $\beta^S/\beta^0$
    c. $\beta^S/\beta^+$;**AND**
C. The individual does not have more than two α-globin gene deletions; **AND**
D. The treatment is prescribed by or in consultation with a hematologist; **AND**
E. The treatment will be administered at an authorized treatment center; **AND**

F. The individual has a history of ≥ 2 severe vaso-occlusive episodes per year in the 2 years prior to screening in the setting of appropriate supportive care defined as:
    a. Acute pain event requiring a visit to a medical facility and administration of pain medications (opioids or intravenous non-steroidal anti-inflammatory drugs [NSAIDs]) or RBC transfusions; **OR**
    b. Acute chest syndrome; **OR**
    c. Priapism lasting >2 hours and requiring a visit to a medical facility; **OR**
    d. Hepatic sequestration; **OR**
    e. Splenic sequestration; **AND**
G. The individual is eligible for a hematopoietic stem-cell transplant (HSCT) as determined by the hematologist; **AND**
H. The individual does not have an available 10/10 human leukocyte antigen-matched related donor; **AND**
I. The individual has not previously received a hematopoietic stem-cell transplant; **AND**
J. The individual has not previously received Lyfgenia or any other gene therapy; **AND**
K. The individual does not have any of the following:
    a. Advanced liver disease as defined by the following:
        1. Alanine transaminase (ALT) >3 × the upper limit of normal (ULN) or direct bilirubin value >2.5 × ULN; **OR**
        2. Baseline prothrombin time (PT) (international normalized ratio [INR]) >1.5 × ULN, **OR**
        3. History of cirrhosis or any evidence of bridging fibrosis, or active hepatitis on liver biopsy; **AND**
    b. A history or presence of Moyamoya disease; **AND**
    c. Bacterial, viral, fungal or parasitic infection including HIV-1, HIV-2, hepatitis B or hepatitis C; **AND**
    d. Any prior or current malignancy or myeloproliferative disorder or a significant immunodeficiency disorder; **AND**
L. The individual has previously trialed at least one pharmacologic treatment for SCD including hydroxyurea, l-glutamine, crizanlizumab-tmca or voxelotor; **AND**
M. The provider will follow all FDA recommendations for usage, dosage, preparation, administration, monitoring and patient education

**Investigational and Not Medically Necessary**

Lyfgenia is considered investigational and therefore not medically necessary for all other indications not specified in this policy.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

**PROCEDURE**
Prior authorization of Lyfgenia is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

**The following information is needed to review requests for Lyfgenia:**

1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program Lyfgenia Prior Authorization Request form (to include physician's order and signature)
2. Clinical documentation supporting the medical necessity of treatment with Lyfgenia should include the following:
    a. Genetic testing confirming:
        i. The diagnosis of sickle cell disease with one of the following genotypes: $\beta^S/\beta^S$, $\beta^S/\beta^0$ or $\beta^S/\beta^+$; **AND**
        ii. The individual does not have more than two α-globin gene deletions; **AND**
    b. Medical record documenting a history of ≥ 2 severe vaso-occlusive episodes per year in prior 2 years; **AND**
    c. Laboratory data confirming the absence of:
        i. HIV-1, HIV-2, HBV, HCV infection; **AND**
        ii. Advanced liver disease; **AND**
    d. Medical record documentation of prior pharmacologic therapies trialed for SCD; **AND**
    e. Signed provider attestation confirming the following:
        i. The individual is eligible for a hematopoietic stem-cell transplant (HSCT); **AND**
        ii. The individual does not have an available 10/10 human leukocyte antigen-matched related donor; **AND**
        iii. The individual has not previously received a HSCT; **AND**
        iv. The individual has not previously received Lyfgenia or any other gene therapy; **AND**
        v. The individual does not have a history or presence of Moyamoya disease; **AND**
        vi. The individual does not have any prior or current malignancy or myeloproliferative disorder or a significant immunodeficiency disorder; **AND**
3. Other information as requested

**Requesting Authorization**
Requests for the prior authorization of Lyfgenia must be submitted by the ordering physician and faxed to the number listed on the request form. Questions regarding this form should be directed to the HUSKY Health Program Utilization Management Department at 1.800.440.5071 (select option for medical authorizations).

**Initial Authorization**
If approved, authorization will be given for a one-time, single-dose intravenous infusion of Lyfgenia.

**Reauthorization**

Lyfgenia is indicated as a one-time infusion only. Repeat administration of Lyfgenia is not supported by FDA labeling or compendia and is therefore not considered medically necessary.

**EFFECTIVE DATE**
This Policy for the prior authorization of Lyfgenia for individuals covered under the HUSKY Health Program is effective May 1, 2025.

**LIMITATIONS**
N/A

**CODES:**

| Code | Definition |
|---|---|
| J3394 | Injection, lovotibeglogene autotemcel, per treatment |

**DEFINITIONS**

1. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
2. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
3. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
4. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
5. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
6. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
7. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
8. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

## ADDITIONAL RESOURCES AND REFERENCES:


- Kanter J, Thompson AA, Pierciey FJ Jr, 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;98(1):11-22. doi:10.1002/ajh.26741
- LYFGENIA [prescribing information], Somerville, MA; bluebird bio, Inc.; December 2023
- Vichinsky EP, Field JJ. Overview of the clinical manifestations of sickle cell disease. In *UpToDate.* DeBaun MR, Tirnauer JS (Eds), Wolters Kluwer. Updated January 23, 2025. Accessed on February 25, 2025


## PUBLICATION HISTORY

| Status | Date | Action Taken |
|---|---|---|
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