NC Medicaid
Prior Approval Criteria
Lyfgenia

Effective Date: July 15, 2025

Therapeutic Class Code: N1K
Therapeutic Class Description: Gene Therapy Agents- CD34+ Hematopoietic Stem Cells

Medication
Lyfgenia (lovotibeglogene autotemcel)

Eligible Beneficiaries
NC Medicaid (Medicaid) beneficiaries shall be enrolled on the date of service and may have service restrictions due to their eligibility category that would make them ineligible for this service.

EPSDT Special Provision: Exception to Policy Limitations for Beneficiaries under 21 Years of

Age 42 U.S.C. § 1396d(r) [1905(r) of the Social Security Act]

Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) is a federal Medicaid requirement that requires the state Medicaid agency to cover services, products, or procedures for Medicaid beneficiaries under 21 years of age **if** the service is **medically necessary health care** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem] identified through a screening examination (includes any evaluation by a physician or other licensed clinician). This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his/her health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems. Medically necessary services will be provided in the most economic mode, as long as the treatment made available is similarly efficacious to the service requested by the beneficiary's physician, therapist, or other licensed practitioner; the determination process does not delay the delivery of the needed service; and the determination does not limit the beneficiary's right to a free choice of providers.

EPSDT does not require the state Medicaid agency to provide any service, product, or procedure

a. that is unsafe, ineffective, or experimental/investigational.
b. that is not medical in nature or not generally recognized as an accepted method of medical practice or treatment.

Service limitations on scope, amount, duration, frequency, location of service, and/or other specific criteria described in clinical coverage policies may be exceeded or may not apply as long as the provider's documentation shows that the requested service is medically necessary "to correct or ameliorate a defect, physical or mental illness, or a condition" [health problem]; that is, provider documentation shows how the service, product, or procedure meets all EPSDT criteria, including to correct or improve or maintain the beneficiary's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT and Prior Approval Requirements

1. If the service, product, or procedure requires prior approval, the fact that the beneficiary is under 21 years of age does **NOT** eliminate the requirement for prior approval.

2. **IMPORTANT ADDITIONAL INFORMATION** about EPSDT and prior approval is found in the *NCTracks Provider Claims and Billing Assistance Guide*, and on the EPSDT provider page. The Web addresses are specified below.

   NCTracks Provider Claims and Billing Assistance Guide:
   https://www.nctracks.nc.gov/content/public/providers/provider-manuals.html

   EPSDT provider page: https://medicaid.ncdhhs.gov/medicaid/get-started/find-programs-and-services-right-you/medicaid-benefit-children-and-adolescents

Clinical Coverage

- Beneficiary is ≥ 12 years of age; **AND**

- Beneficiary has a confirmed diagnosis of sickle-cell disease (includes genotypesβS/βS or βS/β0 or βS/β+ or βS/βC) as determined by 1 of the following:
  - Identification of significant quantities of sickle cell hemoglobin (HbS) with or without an additional abnormal β-globin chain variant by hemoglobin assay; **OR**
  - Identification of biallelic HBB pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing; **AND**

- Beneficiary does NOT have disease with ≥ 2 α-globin gene deletions or non-deletional clinically significant mutations; **AND**

- Beneficiary has failed or has experienced intolerance to hydroxyurea at any point in the past (per healthcare practitioner assessment): **AND**

- Beneficiary has experienced 4 or more VOEs in previous 24 months as determined by the treating clinician **OR** is currently receiving chronic blood transfusions for recurrent VOEs or sickle cell disease associated complications: **AND**

- Beneficiary is a candidate for autologous hematopoietic stem cell transplant (HSCT); **AND**

- Beneficiary does NOT have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40; **AND**

- Beneficiary does NOT have a known 10/10 human leukocyte antigen (HLA) matched related donor willing to participate in an allogeneic HSCT; **AND**

- Beneficiary will be transfused at least twice (once each month) prior to mobilization to reach a target hemoglobin (Hb) of 8-10 g/dL (< 12 g/dL) and HbS < 30%; **AND**

- Beneficiary is HIV negative or HIV positive with negative viral load as confirmed by an HIV test prior to mobilization (Note: See Lygenia prescribing information related to potential drug interactions with anti-retroviral medications and manufacturer recommended tapering of anti-retroviral medications prior to mobilization. Beneficiaries who have received Lyfgenia are likely to test positive by polymerase chain reaction (PCR) assays for HIV due to integrated BB305 LVV proviral DNA, resulting in a possible false-positive PCR assay test result for HIV. Therefore, beneficiaries who have received Lyfgenia should not be screened for HIV infection using a PCR-based assay.); **AND**

- Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative

conditioning; **AND**

- Beneficiary will be monitored for hematologic malignancies periodically after treatment; **AND**
- Lyfgenia must NOT be administered concurrently with live vaccines while immunosuppressed; **AND**
- Must be prescribed in consultation with a board-certified hematologist with Sickle Cell Disease expertise. **AND**
- Beneficiary will NOT receive therapy concomitantly with any of the following:
    - Hydroxyurea for ≥ 2 months prior to mobilization and until all cycles of apheresis are completed (Note: If hydroxyurea is administered between mobilization and conditioning, discontinue 2 days prior to initiation of conditioning); **AND**
    - Myelosuppressive iron chelators (e.g., deferiprone) for 7 days prior to mobilization, conditioning, and 6 months post-treatment; **AND**
    - Disease-modifying agents (e.g., L-glutamine, crizanlizumab) for at least 2 months prior to mobilization; **AND**
    - Prophylactic HIV anti-retroviral therapy (Note: Beneficiaries receiving prophylactic ART should stop therapy for ≥ 1 month prior to mobilization and until all cycles of apheresis are completed); **AND**
    - Mobilization of stem cells using granulocyte-colony stimulating factor (G- CSF); **AND**
    - Erythropoietin for ≥ 2 months prior to mobilization; **AND**

- Beneficiary has NOT received other gene therapy [e.g., Casgevy™ (exagamglogene autotemcel)]**.**

VOE/VOC is defined as an event requiring a visit to a medical facility for evaluation which results in a diagnosis of such being documented due to one (or more) of the following: acute pain, acute chest syndrome, acute splenic sequestration, acute hepatic sequestration, priapism lasting > 2 hours **AND necessitating subsequent interventions such as opioid pain management, non- steroidal anti-inflammatory drugs, RBC transfusion, etc.*

Renewal Criteria

- Coverage will not be renewed

Duration of Approval

- One treatment course

References

1 Lyfgenia [package insert]. Somerville, MA; Bluebird Bio; December 2023.

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Criteria Change Log

07/15/2025	Criteria effective date