Clinical Policy: Lyfgenia - Pharmacy Prior Approval Criteria

Reference Number: WNC.CP.301 Coding Implications
Last Review Date: Revision Log

See Important Reminder **at the end of this policy for important regulatory and legal information.**

Note: When state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Description[1] - This policy discusses medical necessity criteria for Lyfgenia (lovotibeglogne autotemcel) Pharmacy Prior Approval Criteria.

Therapeutic Class Code: N1K

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

Policy/Criteria[1]

I. WellCare of North Carolina® shall cover Lyfgenia when **ALL** the following requirements are met:
- **A.** Member 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;
- **B.** Member is ≥ 12 years of age; **AND**
- **C.** Member 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:
  1. Identification of significant quantities of sickle cell hemoglobin (HbS) with or without an additional abnormal β-globin chain variant by hemoglobin assay; **OR**
  2. Identification of biallelic HBB pathogenic variants where at least one allele is the p.Glu6Val pathogenic variant on molecular genetic testing; **AND**
- **D.** Member does NOT have disease with ≥2 α-globin gene deletions or non-deletional clinically significant mutations; **AND**
- **E.** Member has failed or has experienced intolerance to hydroxyurea at any point in the past (per healthcare practitioner assessment): **AND**
- **F.** Member 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**
- **G.** Member is a candidate for autologous hematopoietic stem cell transplant (HSCT); **AND**
- **H.** Member does NOT have a history of hypersensitivity to dimethyl sulfoxide (DMSO) or dextran 40; **AND**
- **I.** Member does NOT have a known 10/10 human leukocyte antigen (HLA) matched related donor willing to participate in an allogeneic HSCT; **AND**
- **J.** Member 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**

K. Member is HIV negative or HIV positive with negative viral load as confirmed by an HIV test prior to mobilization (Note: See Lyfgenia prescribing information related to potential drug interactions with anti-retroviral medications and manufacturer recommended tapering of anti-retroviral medications prior to mobilization. Members 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, Members who have received Lyfgenia should not be screened for HIV infection using a PCR-based assay.); **AND**

L. Provider has considered use of prophylaxis therapy for seizures prior to initiating myeloablative conditioning; **AND**

M. Member will be monitored for hematologic malignancies periodically after treatment; **AND**

N. Lyfgenia must NOT be administered concurrently with live vaccines while immunosuppressed; **AND**

O. Must be prescribed in consultation with a board-certified hematologist with Sickle Cell Disease expertise. **AND**

P. Member will **NOT** receive therapy concomitantly with any of the following:

1. 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**
2. Myelosuppressive iron chelators (e.g., deferiprone) for 7 days prior to mobilization, conditioning, and 6 months post-treatment; **AND**
3. Disease-modifying agents (e.g., L-glutamine, crizanlizumab) for at least 2 months prior to mobilization; **AND**
4. Prophylactic HIV anti-retroviral therapy (Note: Members receiving prophylactic ART should stop therapy for ≥ 1 month prior to mobilization and until all cycles of apheresis are completed); **AND**
5. Mobilization of stem cells using granulocyte-colony stimulating factor (G- CSF); **AND**
6. Erythropoietin for ≥ 2 months prior to mobilization; **AND**

Q. Member 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.*

II. WellCare of North Carolina® shall **NOT RENEW** coverage.

III. WellCare of North Carolina's® Duration of Approval is **ONE TREATMENT** course.

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2025, American Medical Association. All rights reserved. CPT codes and CPT descriptions are

from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT®* Codes	Description
J3394	Lyfgenia - lovotibeglogne autotemcel

Reviews, Revisions, and Approval	Reviewed Date	Approval Date
Original Approval Date	01/2025	01/2025
Criteria I.E., changed to "Member has failed or has experienced intolerance to hydroxyurea at any point in the past (per healthcare practitioner assessment): AND" Criteria I.F. changed to "Member 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" Criteria I.P.3. deleted "voxelotor." Under NC Guidance/Claims related information, updated state web address.		

References

1. State of North Carolina Medicaid Outpatient Pharmacy Prior Approval Criteria - Lyfgenia. Program Specific Clinical Coverage Policies | NC Medicaid (ncdhhs.gov). Published July 12, 2025. Accessed July 12, 2025.

North Carolina Guidance

Eligibility Requirements

1. An eligible beneficiary shall be enrolled in the NC Medicaid Program (Medicaid is NC Medicaid program, unless context clearly indicates otherwise);
2. Provider(s) shall verify each Medicaid beneficiary's eligibility each time a service is rendered.
3. The Medicaid beneficiary 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 a Medicaid Beneficiary 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 beneficiary 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 practitioner).

This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his or 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:

I. that is unsafe, ineffective, or experimental or investigational.
II. 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 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

- 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.
- **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/

Provider(s) Eligible to Bill for the Procedure, Product, or Service
To be eligible to bill for the procedure, product, or service related to this policy, the provider(s) shall:

i. meet Medicaid qualifications for participation;

ii. have a current and signed Department of Health and Human Services (DHHS) Provider Administrative Participation Agreement; and
iii. bill only for procedures, products, and services that are within the scope of their clinical practice, as defined by the appropriate licensing entity.

Compliance
Provider(s) shall comply with the following in effect at the time the service is rendered:

A. All applicable agreements, federal, state, and local laws and regulations including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements; and
B. All NC Medicaid's clinical (medical) coverage policies, guidelines, policies, provider manuals, implementation updates, and bulletins published by the Centers for Medicare and Medicaid Services (CMS), DHHS, DHHS division(s) or fiscal contractor(s).

Claims-Related Information
Provider(s) shall comply with the NC Tracks Provider Claims and Billing Assistance Guide, Medicaid bulletins, fee schedules, NC Medicaid's clinical coverage policies and any other relevant documents for specific coverage and reimbursement for Medicaid:

- Claim Type - as applicable to the service provided:
  Professional (CMS-1500/837P transaction)
  Institutional (UB-04/837I transaction)
  Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines.
- International Classification of Diseases and Related Health Problems, Tenth Revisions, Clinical Modification (ICD-10-CM) and Procedural Coding System (PCS) - Provider(s) shall report the ICD-10-CM and Procedural Coding System (PCS) to the highest level of specificity that supports medical necessity. Provider(s) shall use the current ICD-10 edition and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for code description, as it is no longer documented in the policy.
- Code(s) - Provider(s) shall report the most specific billing code that accurately and completely describes the procedure, product or service provided. Provider(s) shall use the Current Procedural Terminology (CPT), Health Care Procedure Coding System (HCPCS), and UB-04 Data Specifications Manual (for a complete listing of valid revenue codes) and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for the code description, as it is no longer documented in the policy. If no such specific CPT or HCPCS code exists, then the provider(s) shall report the procedure, product or service using the appropriate unlisted procedure or service code.
  Unlisted Procedure or Service
  CPT: The provider(s) shall refer to and comply with the Instructions for Use of the CPT Codebook, Unlisted Procedure or Service, and Special Report as documented in the current CPT in effect at the time of service.

HCPCS: The provider(s) shall refer to and comply with the Instructions For Use of HCPCS National Level II codes, Unlisted Procedure or Service and Special Report as documented in the current HCPCS edition in effect at the time of service

- Modifiers - Providers shall follow applicable modifier guidelines.
- Billing Units - Provider(s) shall report the appropriate code(s) used which determines the billing unit(s).
- Co-payments -
  For Medicaid refer to Medicaid State Plan:
  https://medicaid.ncdhhs.gov/meetingsnotices/medicaid-state-plan-public-notices

- Reimbursement - Provider(s) shall bill their usual and customary charges. For a schedule of rates, refer to: https://medicaid.ncdhhs.gov/.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise

professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members/enrollees, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.