To all beneficiaries enrolled in a Prepaid Health Plan (PHP): for questions about benefits and services available on or after implementation, please contact your PHP.

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Related Clinical Coverage Policies
Refer to https://medicaid.ncdhhs.gov/ for the related coverage policies listed below:
11A-1, Hematopoietic Stem-Cell Transplantation for Acute Lymphoblastic Leukemia (ALL)
11A-11, Hematopoietic Stem-Cell Transplantation for Non-Hodgkin Lymphomas
1A-39, Routine Costs in Clinical Trial Services for Life Threatening Conditions

1.0 Description of the Procedure, Product, or Service

Engineered T cell–based antitumor immunotherapy uses gene transfer of tumor antigen-specific T-cell receptors (TCR) or synthetic chimeric antigen receptors (CAR). CAR T-Cells are prepared from the beneficiary's peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure. The blood is sent to the manufacturer where the mononuclear cells are enriched for T cells. The T cells are expanded in cell culture, washed, and formulated into a suspension, which then is cryopreserved. This process may take several weeks. The product is then infused into the beneficiary. This technique has shown very encouraging results in clinical trials for treatment of types of leukemias and lymphomas.

1.1 Definitions

a. A **Certified or Authorized Treatment Center** for CAR T-Cell Therapy is a healthcare facility approved to administer CAR T-cell treatments. These centers meet manufacturer and regulatory requirements, including having medical staff trained in the entire CAR T-cell therapy process, from administration to managing potential adverse effects. Certification requires compliance with FDA-mandated training and may be based on a facility's expertise, infrastructure, and ability to treat patients with hematologic malignancies. Only certified or authorized treatment centers can provide specific CAR T-cell therapies, ensuring safe and effective patient care.

b. **Rescue Transplant** - a method of replacing blood-forming stem cells that were destroyed by treatment with high doses of anticancer drugs or radiation therapy. The stem cells help the bone marrow recover and make healthy blood cells. A rescue transplant may allow more chemotherapy or radiation therapy to be given so that more cancer cells are killed. It is usually done using the patient's own stem cells that were saved before treatment. Also called stem cell rescue.

c. **United States Food & Drug Administration (U.S. FDA)** - the Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

2.0 Eligibility Requirements

2.1 Provisions

2.1.1 General

(*The term "General" found throughout this policy applies to all Medicaid policies*)

a. An eligible beneficiary shall be enrolled in the NC Medicaid Program (Medicaid is NC Medicaid program, unless context clearly indicates otherwise).

b. Provider(s) shall verify each Medicaid beneficiary's eligibility each time a service is rendered.

c. The Medicaid beneficiary may have service restrictions due to their eligibility category that would make them ineligible for this service.

2.1.2 Specific

(***The term "Specific" found throughout this policy only applies to this policy***)

a. Medicaid

None Apply.

2.2 Special Provisions

2.2.1 EPSDT Special Provision: Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age

a. **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 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:

1. that is unsafe, ineffective, or experimental or investigational.
2. 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.

b. **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/

3.0 When the Procedure, Product, or Service Is Covered

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

3.1 General Criteria Covered

Medicaid shall cover the procedure, product, or service related to this policy when medically necessary, and:

a. the procedure, product, or service is individualized, specific, and consistent with symptoms or confirmed diagnosis of the illness or injury under treatment, and not in excess of the beneficiary's needs;
b. the procedure, product, or service can be safely furnished, and no equally effective and more conservative or less costly treatment is available statewide; and
c. the procedure, product, or service is furnished in a manner not primarily intended for the convenience of the beneficiary, the beneficiary's caretaker, or the provider.

3.2 Specific Criteria Covered

3.2.1 Specific criteria covered by Medicaid

Medicaid shall cover CAR T-Cell Therapy when **ALL** of the following criteria are met:

a. the CAR T-Cell Therapy has received approval from the United States Food & Drug Administration (U.S. FDA);
b. the CAR T-Cell Therapy is administered per U.S. FDA approved guidelines regarding:
    1. indications and usage;
    2. dosage and administration;
    3. dosage forms and strengths; and
    4. warnings and precautions;
c. the CAR T-cell Therapy is administered at a certified or authorized treatment center. If the therapy is subject to a Risk Evaluation and Mitigation Strategies (REMS) program, the treatment center must be enrolled in the REMS, and providers must be trained on the management of cytokine release syndrome (CRS) and neurological toxicities (refer to **Section 6.2**).

3.2.2 Medicaid Additional Criteria Covered

None Apply.

4.0 When the Procedure, Product, or Service Is Not Covered

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

4.1 General Criteria Not Covered

Medicaid shall not cover the procedure, product, or service related to this policy when:

a. the beneficiary does not meet the eligibility requirements listed in **Section 2.0;**
b. the beneficiary does not meet the criteria listed in **Section 3.0;**
c. the procedure, product, or service duplicates another provider's procedure, product, or service; or
d. the procedure, product, or service is experimental, investigational, or part of a clinical trial.

4.2 Specific Criteria Not Covered

4.2.1 Specific Criteria Not Covered by Medicaid

Medicaid shall not cover CAR T-Cell Therapy for **ANY** one of the following:

a. the CAR T-Cell Therapy has not received approval from the U.S. FDA;
b. the CAR T-Cell Therapy is being administered outside U.S. FDA guidelines regarding:
    1. indications and usage;
    2. dosage and administration; or
    3. dosage forms and strengths;

c. if a CAR T-Cell Therapy requires a Risk Evaluation and Mitigation Strategy (REMS), it is being administered at a facility that has not enrolled in that therapy's REMS program;
d. repeat treatment in beneficiaries who have received another CAR T-Cell Therapy previously;
e. when the beneficiary's psychosocial history limits the beneficiary's ability to comply with pre- and post-infusion medical care; or
f. when there is current beneficiary or caretaker non-compliance that would make compliance with a disciplined medical regime improbable.

4.2.2 Medicaid Additional Criteria Not Covered

Medicaid shall not cover concurrent rescue transplant with infusion of any CAR T-Cell Therapy as this is considered experimental.

5.0 Requirements for and Limitations on Coverage

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

5.1 Prior Approval

Medicaid shall require prior approval for CAR T-Cell Therapy. The provider shall obtain prior approval before rendering CAR T-Cell Therapy.

5.2 Prior Approval Requirements

5.2.1 General

The provider(s) shall submit to the Department of Health and Human Services (DHHS) Utilization Review Contractor the following:

a. the prior approval request; and
b. all health records and any other records that support the beneficiary has met the specific criteria in **Subsection 3.2** of this policy.

5.2.2 Specific

The provider(s) shall submit the following to the Department of Health and Human Services (DHHS) Utilization Review Contractor:

a. Letter of medical necessity **signed by the attending physician,** which documents past chemotherapy regimens and dates, the clinical and social history, and indications for treatment with CAR T-Cell therapy;
b. Verification that the administering facility is a qualified or authorized treatment center for the requested CAR T-Cell Therapy. If this information is publicly available, additional documentation is not required. Otherwise, the provider must submit a copy of the contract between the administering facility and the manufacturer of the requested CAR T-Cell Therapy as confirmation;
c. Serologies (less than three months old) to include Human Immunodeficiency Virus (HIV) and Hepatitis panel (*positive* serology results may be reported that are greater than three months old);

d. All diagnostic and procedure results, including bone marrow biopsy (not more than six months old);
e. Other diagnostic tests may be requested as appropriate; and
f. Complete psychological and social evaluation to include:
    1. beneficiary's medical compliance;
    2. beneficiary's support network;
    3. post-treatment care plan, with identification of primary and secondary care providers; and
    4. history of mental health issues, substance use, or legal issues.

6.0 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:

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

6.1 Provider Qualifications and Occupational Licensing Entity Regulations

None Apply.

6.2 Provider Certifications

Due to the risk of cytokine release syndrome (CRS) and neurological toxicities, certain CAR T-Cell Therapies are only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). A REMS is a program to manage known or potential serious risks associated with a drug product and is required by the U.S. Food & Drug Administration (U.S. FDA) to ensure that the benefits of the drug outweigh its risks.

If a CAR T-Cell Therapy requires a REMS, the goals of the REMS are to mitigate the risks of CRS and neurological toxicities by:

a. Ensuring that hospitals and their associated clinics that dispense CAR T-Cell Therapies are specially certified and have on-site, immediate access to tocilizumab; and
b. Ensuring those who prescribe, dispense, or administer CAR T-Cell Therapies are aware of how to manage the risks of cytokine release syndrome and neurological toxicities.

NOTE: If a CAR T-Cell Therapy is subject to a REMS, hospitals and their associated clinics must be certified and enrolled in the therapy's respective REMS to administer the treatment.

7.0 Additional Requirements

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

7.1 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).

8.0 Policy Implementation and History

Original Effective Date: December 1, 2019

History:

Date	Section or Subsection Amended	Change
12/01/2019	All Sections and Attachment(s)	New Clinical Coverage Policy documenting criteria for CAR-T Cell Therapy involving the administration of tisagenlecleucel (KYMRIAH) and axicabtagene ciloleucel (YESCARTA).
12/01/2019	Attachment A	Updated policy template language "Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines".
12/01/2019	Table of Contents	Updated policy template language, "To all beneficiaries enrolled in a Prepaid Health Plan (PHP): for questions about benefits and services available on or after implementation, please contact your PHP."
10/01/2021	Section 1.0	Descriptions of specific CAR T-Cell Therapies removed.
10/01/2021	Section 1.1	Definition added for U.S. FDA.
10/01/2021	Section 3.2.1	Removed listing of specific CAR T-Cell Therapies. Added coverage statement for FDA approved CAR T-Cell Therapies when administered per FDA approved guidelines.
10/01/2021	Section 4.2.1	Removed listing of specific CAR T-Cell Therapies. Added non-coverage statement for CAR T-Cell Therapies. Sections 4.2.3 and 4.2.4 absorbed here.
10/01/2021	Section 4.2.2	Removed listing of specific CAR T-Cell Therapies.
10/01/2021	Section 4.2.3	Section removed and information moved to Section 4.2.1
10/01/2021	Section 4.2.4	Section removed and information moved to Section 4.2.1
10/01/2021	Section 5.2.2	Added "other diagnostic tests may be requested as appropriate" to specific prior approval requirements.
10/01/2021	Section 5.3	Information moved to Attachment A.
10/01/2021	Section 6.2	Removed listing of specific CAR T-Cell Therapies.
10/01/2021	Attachment A	Specific ICD-10 CM, ICD-10 PCS, and HCPCS codes removed. Specific NDCs removed. Revised criteria on requirements to submit 30-day patient response to

Date	Section or Subsection Amended	Change
		therapy with claim. This is only required for KYMRIAH for ALL.
08/15/2023	All Sections and Attachments	Updated policy template language due to North Carolina Health Choice Program's move to Medicaid. Policy posted 08/15/2023 with an effective date of 4/1/2023.
04/01/2025	Section 1.1	Definition added for Certified or Authorized Treatment Center.
04/01/2025	Section 3.2.1	Language updated to reflect that only CAR T-Cell Therapies with an FDA-required REMS will require facility participation in the REMS program.
04/01/2025	Section 4.2.1	Language updated to reflect that only CAR T-Cell Therapies with an FDA-required REMS will require facility participation in the REMS program.
04/01/2025	Section 5.2.2	Clarified that facility-manufacturer contracts are only required to verify certification or authorization as a treatment center if this information is not publicly available on the website.
04/01/2025	Section 6.2	Language updated to reflect that only CAR T-Cell Therapies with an FDA-required REMS will require facility participation in the REMS program.

Attachment A: Claims-Related Information

Provider(s) shall comply with the, *NCTracks 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:

A. Claim Type

Institutional (UB-04/837I)

Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines.

B. 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.

a. Provider(s) shall file inpatient claims for CAR T-Cell Therapy with the **product-specific** ICD-10 PCS code, if one has been assigned. If a product-specific ICD-10 PCS has not been assigned, provider(s) shall file inpatient claims with the most specific available billing code.
b. Provider(s) shall include the prior authorization (PA) number on the claim.
c. Provider(s) shall attach invoice from manufacturer of CAR T-Cell Therapy.
d. If the CAR T-Cell Therapy administered is KYMRIAH (tisagenlecleucel) for B-cell precursor acute lymphoblastic leukemia (ALL), provider(s) shall attach documentation with the claim regarding 30-day beneficiary response.

C. 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.

Revenue Code(s)
0636

HCPCS Code(s)
C9399

a. Provider(s) shall file outpatient claims for CAR T-Cell Therapy with **Revenue Code 0636** and the **product-specific** HCPCS code for the CAR T-Cell Therapy. If the CAR T-Cell Therapy has been approved by the U.S. FDA but has not yet been assigned a product-specific HCPCS code, the provider shall use HCPCS C9399 (UNCLASSIFIED DRUGS OR BIOLOGICALS).
b. Provider(s) shall include the prior authorization (PA) number on the claim.
c. Provider(s) shall attach invoice from manufacturer of CAR T-Cell Therapy.
d. If the CAR T-Cell Therapy administered is KYMRIAH (tisagenlecleucel) for B-cell precursor acute lymphoblastic leukemia (ALL), provider(s) shall attach documentation with the claim regarding 30-day beneficiary response.

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.

D. Modifiers

Provider(s) shall follow applicable modifier guidelines.

Provider(s) billing for 340B drugs shall bill the cost that is reflective of their acquisition cost.

Provider(s) shall indicate that a drug was purchased under a 340B purchasing agreement by appending the **"UD" modifier** on the drug detail.

E. Billing Units

Provider(s) shall report the appropriate code(s) used which determines the billing unit(s).

Providers must bill National Drug Codes (NDCs) and appropriate NDC units.

The NDC units must be reported as "UN1."

F. Place of Service

Inpatient Hospital, Outpatient Hospital.

G. Co-payments

For Medicaid refer to the NC Medicaid State Plan:
https://medicaid.ncdhhs.gov/meetings-notices/medicaid-state-plan-public-notices

H. Reimbursement

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