Clinical Policy: Thymus Tissue Implantation

Reference Number: WNC.CP.279
Last Review Date: 05/24

Coding Implications
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.

PLEASE NOTE: This service REQUIRES Medical Director Review.

Description[1]

Congenital athymia is a rare immune disorder in which a child is born without a thymus – an organ that plays a critical role in helping the body learn to fight infections. Children impacted by this disease typically die within the first two years of life and may have repeated, often life-threatening infections due to the lack of adequate working T cells.

This policy addresses thymus tissue implantation (also known as culture thymus tissue [CTT] implantation) using allogeneic processed thymus tissue (allogeneic processed thymus tissue-agdc [RETHYMIC®], Enzyvant Therapeutics, Inc. Cambridge, MA) a regenerative therapy used for immune reconstitution in children with congenital athymia.

Policy/Criteria[1]

I. WellCare of North Carolina® **shall cover** a single administration of allogeneic processed thymus tissue for immune reconstitution in a Member who is 17 years of age and younger with congenital athymia when **ALL** of the following criteria are met:
- **A.** Congenital athymia is confirmed via a circulating T-cell count on flow cytometry demonstrating fewer than 50 naïve T cells/mm3 (CD45RA+, CD62L+) in the peripheral blood **or** less than 5 percent of total T cells being naïve in phenotype;
- **B.** Documentation that infection control measures, consisting of immunoprophylaxis and withholding of immunizations, can reasonably be maintained until the development of thymic function is established;
- **C.** Absence of comorbidities, in the opinion of the treating clinician, that are reasonably likely to result in severe complications, including death from administration of allogeneic processed thymus tissue (such as pre-existing renal impairment, or cytomegalovirus or Epstein-Barr virus infection); AND
- **D.** HLA matching is required, performed and documented in a Member who has received a prior hematopoietic cell transplantation (HCT) or a solid organ transplant.

II. It is the policy of WellCare of North Carolina®**, shall NOT cover** the use of allogeneic processed thymus tissue for administration of all other uses, including:

A. Immune reconstitution in a Member with severe combined immunodeficiency (SCID); **and**
B. Repeat administration in a Member who has previously received allogeneic processed thymus tissue.

III. Limitations: WellCare of North Carolina®**, shall** require prior approval for Thymus Tissue Transplantation.
A. The provider shall obtain prior approval before rendering Thymus Tissue Implantation.
B. Continued therapy is not authorized as it is to be dosed one time only.
C. Thymus Tissue Implantation is once per lifetime.

IV. Documentation Requirements:
A. Letter of medical necessity **signed by the attending physician**, which documents the member's medical history, absence of significant comorbidities, and indications for treatment with Thymus Tissue Implantation;
B. Lab results confirming congenital athymia as described in Criteria I. of this policy;
C. Documentation that infection control measures, consisting of immunoprophylaxis and withholding of immunizations, can reasonably be maintained until the development of thymic function is established; and
D. Documentation that HLA matching has been performed in a Member who has received a prior hematopoietic cell transplantation (HCT) or a solid organ transplant.

V. Place of Service:
A. Inpatient Hospital

Background[1]
RETHYMIC is composed of human allogeneic thymus tissue that is processed and cultured, and then implanted into the Member to help reconstitute immunity. Dosing is patient customized, determined by the surface area of the RETHYMIC slices and the body surface area of the Member.

Definitions:
Allogeneic - Allogeneic refers to the transplantation or transfer of cells, tissues, or organs between individuals of the same species who are genetically different. This process is also known as allograft or allogenic transplantation.

Flow Cytometry - Flow cytometry is a laboratory technique that quantifies the number of cells, live cell percentage, and specific cell characteristics, such as size and shape, in blood, bone marrow, or other tissue. Additionally, it detects the presence of tumor markers, such as antigens, on cell surfaces. During the process, cells are stained with a photosensitive dye, suspended in a fluid, and analyzed individually as they pass through a light beam. The measurements are based

on how the stained cells interact with the beam of light. Flow cytometry is a valuable tool for both basic research and the diagnosis and management of various diseases, including cancer.

Hematopoietic Stem Cell Transplant - Hematopoietic stem cell transplant is a medical process in which a Member receives healthy stem cells to replace their own stem cells that have been destroyed by high doses of chemotherapy or radiation treatment. Healthy stem cells may originate from the member's blood or bone marrow, or they may come from a related or unrelated donor. Depending on the source of the stem cells, the transplant may be categorized as autologous, allogenic, syngeneic, or cord blood.

Human leukocyte antigen (HLA) - Human leukocyte antigen (HLA) is a type of molecule that is present on the surface of most cells in the body. These molecules play a vital role in the immune response of the body against foreign substances. HLAs are responsible for a person's tissue type, which is unique to each individual. Before a stem cell or organ transplant, HLA tests are conducted to determine if there is a match between the donor and the recipient's tissues. Human lymphocyte antigen is another term used to refer to HLAs.

HLA Matching - HLA matching is a procedure that involves analyzing blood or tissue samples to identify human leukocyte antigens (HLAs). HLAs are molecules that are present on the surface of most cells in the body and they determine a person's unique tissue type. These molecules are crucial for the immune system's response to foreign substances. Before a stem cell or organ transplant, HLA matching is performed to determine if there is compatibility between the donor and the recipient's tissues. Human lymphocyte antigen matching is another term used to refer to HLA matching.

Immunoprophylaxis - The process of preventing disease through the creation of active or passive immunity.

Phenotype - Phenotype refers to the observable physical, biochemical, and behavioral characteristics that are present in an individual.
Some examples of a person's phenotype include their height, eye color, hair color, blood type, behavior, and the presence of certain diseases. Phenotypic traits are determined by a combination of genetic factors and environmental influences, such as diet, exercise, and smoking.

Thymus – The Thymus is an organ that is part of the lymphatic system, in which T lymphocytes grow and multiply. This process is crucial in helping the body develop the ability to fight off infections. Located in the chest behind the breastbone, the thymus plays a vital role in immune function.

T-Cell - T cells, also known as T lymphocytes or thymocytes, are a type of white blood cell that originate from stem cells in the bone marrow and are essential components of the immune system. T cells play a vital role in protecting the body against infections, and they may also assist in fighting cancer..

Coding Implications

CPT®* Codes	Description
60699	Unlisted procedure, endocrine system

HCPCS ®* Codes	Description
Non-Applicable	

ICD-10-PCS Code that Support Coverage Criteria

+ Indicates a code(s) requiring an additional character

ICD-10-PCS Code	Description
XW020D8	INTRODUCTION OF ENGINEERED ALLOGENEIC THYMUS TISSUE INTO MUSCLE, OPEN APPROACH, NEW TECHNOLOGY GROUP 8

Reviews, Revisions, and Approvals	Reviewed Date	Approval Date
Original Approval date.	05/23	05/23
CPT code 60699 added. Definitions updated with no effect on criteria.	11/23	11/23
Annual Review.	05/24	05/24

References

1. State of North Carolina Medicaid. Medicaid and Health Choice Clinical Coverage Policy No:11B-9 Thymus Tissue Implantation. Program Specific Clinical Coverage Policies | NC Medicaid (ncdhhs.gov). Published August 15, 2023. Accessed March 1, 2024.

North Carolina Guidance

Eligibility Requirements

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.

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 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:

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.

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/

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.

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:

a. 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.
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.
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.
   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 - Providers shall follow applicable modifier guidelines.
e. Billing Units - Provider(s) shall report the appropriate code(s) used which determines the billing unit(s).
f. Co-payments -
For Medicaid refer to Medicaid State Plan:
https://medicaid.ncdhhs.gov/get-involved/nc-health-choice-state-plan

g. 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.