Molina Clinical Policy
Allogeneic Processed Thymus Tissue–agdc (Rethymic)
Policy No. 472

Last Approval: 06/11/2025
Next Review Due By: June 2026

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Congenital athymia, the complete lack of or a severely reduced functional thymus at birth, is a rare primary immunodeficiency condition. The thymus is an integral part of the immune system, as it is responsible for maturing and training T lymphocytes, also known as T cells. While there are different types of T cells, their general role in the body is to identify pathogens and, once activated, kill the invading infection. Without a functioning thymus and subsequent T cells the body is easily overwhelmed with pathogens, leading to life threatening infections in children with congenital athymia. This condition is associated with multiple congenital conditions such as complete DiGeorge Syndrome, CHARGE Syndrome, FOXN1 Deficiency, and diabetic embryopathy (NORD 2024).

Rethymic is a custom engineered allogenic donor thymus tissue intended as a curative treatment for congenital athymia. Rethymic takes approximately two to three weeks to be developed, after which it is ready for implantation. The implantation procedure is a one-time surgical treatment in which the engineered thymus tissue is placed into one or both thighs of the pediatric patient. Once implanted, the highly vascularized thigh muscle promotes and sustains perfusion to newly implanted thymus tissue. The patient's naïve T cells migrate from the bone marrow to the implanted thymus tissue leading to immune reconstitution. Sufficient immune reconstitution takes approximately 6 to 12 months post implant, with some patients not achieving sufficient infection protection until 2 years after the procedure. Before laboratory confirmation of appropriate immune function, strict implementation of infection control measures must continue for the safety of the patient (Rethymic 2024).

Regulatory Status
Rethymic (Enzyvant Therapeutics GmbH) is currently the only FDA approved allogeneic processed thymus tissue–agdc. It is regulated as a Vaccine, Blood & Biologics product under the STN 125685. Rethymic gained initial FDA approval on October 8, 2021.

COVERAGE POLICY

Allogeneic Processed Thymus Tissue–agdc (Rethymic) administration may be **considered medically necessary** as a *one-time* procedure when ALL the following criteria are met:

1. Member is 17 years or younger
2. Member has diagnosis of congenital athymia and ONE of the following:
   a. T-cell count lower than 50/mm^3 confirmed via flow cytometry
   b. Naive T-cell (CD3+CD4+CD45RA+CD62L+ or CD3+CD8+CD45RA+ CD62L+ cells) count lower than 50/mm3 (less than 5% of total T cells being naïve in phenotype)
3. Documented attestation that Member's caregivers understand necessity of and can enforce strict infection control measures until the development of thymic function is established

4. Absence of ALL the following contraindications:
    a. Severe combined immunodeficiency (SCID)
    b. Pre-existing cytomegalovirus infection (CMV) or human immunodeficiency virus (HIV) infection
    c. Previous thymus transplantation

Continuation of Therapy
Allogeneic Processed Thymus Tissue–agdc (Rethymic) administration is intended as a *once in a lifetime treatment*. Subsequent administration is considered **experimental, investigational, and unproven** due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Non-Randomized Studies, Retrospective Reviews, and Other Evidence
Markert et al. (2022) published the results of a collection of ten prospective, single-arm open-label studies, spanning 27 years, analyzing patients before and after the administration of cultured thymus tissue (CTT). A total of 105 patients were enrolled and received CTT, of which 95 had treatment naïve athymia. Inclusion criteria were absent genetic defects associated with severe combined immunodeficiency syndrome, and confirmation of athymia via results of a circulating $CD3^+CD45RA^+CD62L^+$ T-cell count lower than 50/mm^3 or less than 5% of the total T-cell count on 2 separate flow cytometry analyses performed at 3 months and 1 month prior to administration of CTT. CTT was administered in the quadriceps muscle of one or both thighs. Post CTT administration, patients received IgG replacement, prophylactic antimicrobials, and immunosuppressant therapy until immune reconstitution was established.

Of the 105 patients enrolled, 95 of them were in the efficacy analysis set. Ten patients were ultimately excluded due to a diagnosis of SCID in 2 patients, an indefinite diagnosis of athymia in 2 patients, and 6 patients having received previous transplant therapy prior to CTT administration. The Kaplan-Meier estimated survival rates at year 1 and year 2 were 77% and 76%, respectively. Of the patients alive a year post CTT administration, there was an estimated survival rate of 93% at the median follow-up time of 10.9 years. A total of 28 deaths were documented, of which 22 of those deaths (including 12 of the 13 infection-related deaths) occurred in the first year after administration of CTT while the patients were still immunodeficient. The 3 deaths occurring after the second-year post CTT administration were not related to immunodeficiency, which implies that patients without life-threatening comorbidities who survive past 2 years will likely survive into adulthood.

CTT acts similarly to normal thymus tissue to produce naïve T cells that then go on to fight infections in the peripheral blood, as evidence by CTT being found in 25 of the 30 biopsy specimens examined with all but 2 demonstrating thymopoiesis. The median T-cell counts reached their peak at approximately 1 to 2 years after CTT administration, with naive T-cell numbers starting at 0 in all patients and subsequently increasing until reaching their highest numbers in year 2. Immune reconstitution sufficient to fight infection typically developed between 6 to 12 months post CTT administration. In summation, children with untreated athymia typically die within the first few years of life due to life threatening infection; therefore, CTT administration increases survival rates compared to those with untreated athymia.

National/Specialty Organizations
The **American Academy of Allergy, Asthma & Immunology (AAAAI)** and the **American College of Allergy, Asthma & Immunology (ACAAI)** issued a joint practice parameter, the *Practice Parameter for the Diagnosis and Management of Primary Immunodeficiency* (Bonilla et al. 2015). Summary 63 in the parameter states “Treatment of infants with complete DGS [DiGeorge Syndrome] requires some form of T-cell reconstitution… Reconstitution of T-cell function in infants with complete DGS and CHARGE syndrome has been accomplished through transplantation of fetal thymus tissue, postnatal thymus tissue, HLA-identical sibling HSCT, and peripheral blood mature T-cell transplantation.”

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
60699	Unlisted procedure, endocrine system [when specified as implantation of Rethymic (allogeneic processed thymus tissue–agdc)]

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Rethymic (allogeneic processed thymus tissue–agdc)]
J3590	Unclassified biologics biologicals [when specified as Rethymic (allogeneic processed thymus tissue–agdc)]

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

06/11/2025 New policy. IRO Peer Reviewed on May 20, 2025 by a practicing physician board certified in Pediatric Allergy & Immunology.

REFERENCES

1. Bonilla FA, Khan DA, Ballas ZK, et al.; Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma & Immunology; the American College of Allergy, Asthma & Immunology; and the Joint Council of Allergy, Asthma & Immunology. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015 Nov;136(5):1186-205.e1-78. doi: 10.1016/j.jaci.2015.04.049. Epub 2015 Sep 12. PMID: 26371839.
2. Markert ML, Gupton SE, McCarthy EA. Experience with cultured thymus tissue in 105 children. J Allergy Clin Immunol. 2022 Feb;149(2):747-757. doi: 10.1016/j.jaci.2021.06.028. Epub 2021 Aug 4. PMID: 34362576; PMCID: PMC8810898.
3. National Organization for Rare Diseases (NORD). Congenital Athymia. Updated October 10, 2024. Accessed May 9, 2025. https://www.rarediseases.org.
4. Rethymic. About Rethymic. Updated November 2024. Accessed May 9, 2025. https://www.rethymic.com/what-is-rethymic/.
5. United States Food and Drug Administration (FDA). Vaccines, Blood & Biologics. RETHYMIC. STN 125685. Accessed May 9, 2025. https://www.fda.gov/vaccines-blood-biologics/rethymic.