Policy Number	RX501.139
Policy Effective Date	06/15/2024

Allogeneic Processed Thymus Tissue-agdc (Rethymic)

Table of Contents
Coverage
Policy Guidelines
Description
Rationale
Coding
References
Policy History

Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current peer-reviewed scientific literature. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and acceptable standards of medical practice. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For Illinois only: Illinois Public Act 103-0458 [Insurance Code 215 ILCS 5/356z.61] (HB3809 Impaired Children) states all group or individual fully insured PPO, HMO, POS plans amended, delivered, issued, or renewed on or after January 1, 2025 shall provide coverage for therapy, diagnostic testing, and equipment necessary to increase quality of life for children who have been clinically or genetically diagnosed with any disease, syndrome, or disorder that includes low tone neuromuscular impairment, neurological impairment, or cognitive impairment.

Coverage

Rethymic (allogeneic processed thymus tissue-agdc) **may be considered medically necessary** for immune reconstitution in pediatric patients ages 3 years or younger with congenital athymia when all of the following criteria are met:

- Patient has a diagnosis of congenital athymia confirmed by a pediatric immunologist; AND
- Patient does NOT have a diagnosis of severe combined immunodeficiency (SCID); AND
- Medical record documentation confirming the patient does NOT have pre-existing cytomegalovirus (CMV) infection OR human immunodeficiency virus (HIV) infection; AND
- Patient has not previously been treated with Rethymic; AND
- Diagnosis of congenital athymia has been confirmed with documentation of the following:
    - Flow cytometry results demonstrating fewer than 50 naïve T-cells/mm^3 ($CD45RA^+$, $CD62L^+$) in the peripheral blood or less than 5% of total T-cells being naïve in phenotype; AND
    - One of the following:
        - Genetic testing confirms 22q11.2 deletion; OR
        - Hematopoietic stem cells (HSCs) successfully differentiate using artificial thymic organoid (ATO) system test; OR
        - Patient has syndromic comorbidities (e.g., palatal anomalies, cardiac abnormalities, hypocalcemia, hearing loss, coloboma, etc.) associated with congenital athymia; AND
    - Patient has documentation of screening for anti-HLA antibodies.

Rethymic (allogeneic processed thymus tissue-agdc) **is considered not medically necessary** in patients with pre-existing cytomegalovirus (CMV) infection or human immunodeficiency (HIV) infection or have been previously treated with Rethymic.

Dosing and Administration
The Rethymic implantation will not exceed a single, one-time dose (up to 22,000 mm^2 of Rethymic surface area per m^2 recipient body surface area (BSA), not to exceed 42 slices) as calculated and supplied by the manufacturer.

Rethymic (allogeneic processed thymus tissue-agdc) **is considered experimental, investigational and/or unproven** for all other indications.

NOTE 1: This policy is specific to the allogeneic processed thymus tissue-agdc known as Rethymic. Comprehensive discussion regarding the conditions resulting in congenital athymia is out of scope for this policy.

Policy Guidelines

None.

Description

Congenital Athymia

Congenital athymia (CA) is an ultra-rare disorder characterized by the absence of the thymus at birth. The thymus is crucial for the maturation and selection of T cells; infants born without a thymus suffer from profound immunodeficiency. Congenital athymia is often first identified through newborn screening for severe combined immunodeficiency (SCID), required in all 50 states in the United States (U.S.). Approximately 20 children are born with CA annually in the U.S. (3, 4)

Multiple genetic abnormalities, congenital syndromes, and environmental factors are associated with congenital athymia, and the care of these infants is complex. While 22q11.2 deletion-associated with DiGeorge Syndrome (DGS) is the most common genetic defect associated with CA, FOXN1, PAX1, and others have also been identified as potentially causative. Among patients with DGS, the majority have partial DGS (pDGS), which is characterized by T cell deficiency, but not athymia. Complete DGS (cDGS) refers to patients with CA; cDGS patients account for a minor proportion of all DGS patients. CHARGE Syndrome (Coloboma, Heart defects, Atresia of the nasal choanae, Retardation of growth and development, Genitourinary anomalies, and Ear anomalies) has also been shown to be associated with CA. (3)

The absence or underdevelopment of the thymus results in an increased susceptibility to viral, fungal, and bacterial infections. Respiratory infections are common as are opportunistic infections caused by microorganisms that usually do not cause disease in individuals with fully functioning immune systems, or widespread systemic disease caused by microorganisms that typically cause only localized, mild infections. While these infants are more susceptible to infections, their bodies also cannot effectively fight off these infections. (2)

Pneumonias caused by *Pseudomonas* spp including *P. aeruginosa*, as well as *C. albicans, S. aureus, S. pneumoniae*, and Haemophilus parainfluenza tend to occur at a high rate in these patients. Chronic lung disease can develop because of recurrent and severe infections. Gastrointestinal infections are also frequent among this population, including rotavirus, norovirus, enterovirus, *M. bovis*, and *C. difficile* infections. These infections can lead to failure to thrive, malabsorption, and diarrhea. Infections of the urinary tract from *K. pnuemoniae, E. faecium*, and echovirus have been reported, as well as infections of the head, ears, nose, and throat including meningitis, sinusitis, mastoiditis, and thrush. Athymic patients can also experience sepsis, which can be associated with mortality for this patient population. (3)

It is critical to ensure that these infants do not receive immunizations prior to immune reconstitution as live vaccines may be fatal. Hematopoietic stem cell transplantation has not proved effective in treating these patients. (3)

Rethymic
Rethymic (allogeneic processed thymus tissue-agdc) is composed of yellow to brown slices of processed and cultured thymus tissue supplied adhered to filter membranes. The slices are teased away from the filters prior to surgical implantation into thigh muscle. It is intended to function as if it is a normal endogenous thymus. Its thymic endothelial cells recruit immature host T cells (thymocytes) into the slices where they undergo further maturation and positive and negative selection, releasing into circulation immunocompetent naive T-cells that can provide protection from infection. (4)

Rethymic is manufactured from allogeneic-unrelated donor thymus tissue that is collected from donors <9 months of age who are undergoing heart surgery. The product is manufactured on demand, and although a product lot is intended for a specific patient, HLA-matching of donor and recipient is not performed, and the product lot can be targeted to a different patient if needed if the dosage is consistent with the body surface area of a different patient. The thymus tissue slices are collected for transplantation after 12 to 21 days of culture. The primary purpose of the manufacturing process is to greatly reduce viable allogeneic thymocyte levels within the tissue slices for safety reasons, while maintaining similar overall tissue organization, viability, and retention of important cell types believed to be important for product function. (4)

Rethymic is administered by a surgical procedure and is implanted into the quadriceps muscle. The dosage is determined by the total surface area of the Rethymic slices and recipient body surface area (BSA). A Rethymic slice is defined as the contents on a single filter membrane; the Rethymic slices are variable in size and shape. The recommended dose range is 5,000 to 22,000 mm^2 of Rethymic surface area/m^2 recipient BSA. The manufacturer calculates the dose in advance for the specific patient; the amount of product provided is adjusted at the manufacturing facility to ensure the maximum dose for the patient cannot be exceeded. Up to 42 cultured Rethymic slices will be provided for each patient. At the time of surgery, the manufacturing personnel communicate to the surgical team the portion of the product that represents the minimum dose. Patients with evidence of maternal engraftment or an elevated response to phytohemagglutinin (PHA) should receive Rethymic with immunosuppressive medications. (1)

Regulatory Status
The U. S. Food and Drug Administration (FDA) approved a Biologics License Application (BLA) for Rethymic (Enzyvant Therapeutics GmbH, Basel, Switzerland) for immune reconstitution in pediatric patients with congenial athymia on October 8, 2021. Table 1 provides a snapshot of the regulatory history.

Table 1. Regulatory History of Rethymic (4)

Regulatory Events/Milestones	Date
IND Submission	May 28, 2001
Orphan Drug designation granted	August 15, 2003
Breakthrough Therapy designation granted	April 13, 2017

Regenerative Medicine Advanced Therapy designation granted	April 13, 2017
Rare Pediatric Disease designation granted	April 5, 2019
BLA filed	June 4, 2019
Approval granted	October 8, 2021

Adapted from: FDA – October 8, 2021 Rethymic Summary Basis for Regulator Action
IND: investigational new drug; BLA: Biologics License Application

Rationale

This medical policy was developed in November 2021 and is based on information retrieved from the U.S. Food and Drug Administration (FDA) website and a literature search of the PubMed database.

Rethymic (1)
The efficacy of Rethymic was evaluated in 10 prospective, single-center, open-label studies that enrolled a total of 105 patients, including 95 patients in the primary efficacy analysis. The demographics and baseline characteristics of the patients enrolled in the clinical studies were similar across studies. Across the efficacy population, 59% were male; 70% were White, 22% were Black, 4% were Asian/Pacific Islander; 2% were American Indian/Alaskan Native; and 2% were multi-race. The median (range) age at the time of treatment was 9 months (1-36). The diagnosis of congenital athymia was based on flow cytometry documenting fewer than 50 naïve T cells/mm^3 (CD45RA+, CD62L+) in the peripheral blood or less than 5% of total T cells being naïve in phenotype in 91/95 patients (range 0-98 naïve T cells/mm^3). In addition to congenital athymia, patients also had complete DiGeorge syndrome (cDGS; also referred to as complete DiGeorge anomaly (cDGA)) if they also met at least one of the following criteria: congenital heart defect, hypoparathyroidism (or hypocalcemia requiring calcium replacement), 22q11 hemizygosity, 10p13 hemizygosity, CHARGE (coloboma, heart defect, choanal atresia, growth and development retardation, genital hypoplasia, ear defects including deafness) syndrome, or CHD7 mutation. Across the efficacy population, 93 patients (98%) were diagnosed with cDGS, and the most common DiGeorge gene mutations or syndromic associations were Chromosome 22q11.2 deletion (36 patients; 38%) and CHARGE syndrome (23 patients; 24%). There were 35 patients with missing or no identified genetic mutations. Two (2%) patients had FOXN1 deficiency, and 1 patient (1%) had a TBX variant. There were 50 (53%) patients with typical cDGS; these patients had congenital athymia with the absence of a T cell-related rash. There were 42 (44%) patients diagnosed with atypical cDGS; these patients may have had a rash, lymphadenopathy, or oligoclonal T cells. Patients who did not have congenital athymia (e.g., SCID) and patients with prior transplants, including thymus and HCT, were excluded from the efficacy analysis population. The baseline demographics and disease characteristics were similar in the safety population.

Patients with heart surgery anticipated within 4 weeks prior to, or 3 months after, the planned

Rethymic treatment date, patients with human immunodeficiency virus (HIV) infection, and patients who were not considered good surgical candidates were excluded from study participation.

Patients in the efficacy population received Rethymic in a single surgical procedure at a dose of 4,900 to 24,000 mm^2 of Rethymic / recipient BSA in m^2. Patients were assigned to receive 16 immunosuppressive therapies prior to and/or after treatment according to their disease phenotype and pre-Rethymic PHA response. Table 2 summarizes the criteria used to administer immunosuppression. Table 3 summarizes the specific immunosuppressant dosing used in Rethymic clinical studies. No patients were retreated with Rethymic.

Table 2. Summary of Treatment Assignment to Immunosuppression During Clinical Studies

Complete DiGeorge Anomaly Phenotype	**Phytohemagglutinin (PHA) Response[1]**	**Immunosuppression Used During Clinical Studies with Rethymic**
Typical	< 5,000 cpm or < 20-fold response to PHA over background	None
Typical	> 5,000 cpm and < 50,000 cpm or Evidence of maternal engraftment	• ATG-R • Methylprednisolone
Typical	> 50,000 cpm	• ATG-R • Methylprednisolone • Cyclosporine[2]
Atypical	< 40,000 cpm on immunosuppression or < 75,000 cpm when not on immunosuppression	• ATG-R • Methylprednisolone • Cyclosporine[2]
Atypical	> 40,000 cpm on immunosuppression or > 75,000 cpm when not on immunosuppression or Evidence of maternal engraftment	• ATG-R • Methylprednisolone • Cyclosporine[2] • Basiliximab[3] • MMF[4]

ATG-R: anti-thymocyte globulin [rabbit] (Thymoglobulin); cpm: counts per minute; MMF: mycophenolate mofetil; PHA: phytohemagglutinin.

[1] Values for PHA response are reported from Duke University Medical Center and may not be comparable to values reported at other clinical laboratories. A patient background value (cells without stimulus) of less than 5,000 cpm was required to consider PHA test results valid. A normal control value of > 75,000 cpm was also required during clinical studies.

[2] If the patient could not tolerate cyclosporine due to adverse events (AEs), then the immunosuppression could have been changed to tacrolimus.
[3] Basiliximab could have been given 24 hours prior to Rethymic administration for activated T cells (> 200 cells/mm^3 or > 50% T cells expressing CD25+) persisting after ATG-R administration. Post-implantation, if the T cell count was > 2000 cells/mm^3 and > 50% of T cells were expressing CD25+, a single dose of basiliximab could be given if not previously administered.
[4]MMF could have been given if T cells remained elevated 5 days after ATG-R administration. MMF was stopped after 35 days if there was no extensive rash and if the aspartate aminotransferase and alanine aminotransferase were less than 3x the upper limit of normal and if T cells were < 5,000 cells/mm^3. If these criteria were not met, MMF could have been continued for up to 6 months.

Table 3. Summary of Immunosuppressant Dosing During Clinical Studies

Immunosuppressant	Dose of Immunosuppressant

ATG-R	• 2 mg/kg IV administered once per day for 3 consecutive days pre-implantation (3 total doses)
	• Administered over ~12 hrs starting at 0.125 ml/kg/hr into a central line for 1 hr, then 0.25 mL/kg/hr x 1 hr, then 0.35 mg/kg/hr for remainder of the infusion
	• Rethymic implantation occurred within 7 days of last dose of ATG-R
	  ○ If the implant occurred more than 7 days after the last dose of ATG-R, a T cell count was repeated.
	  ○ If the T cell count was <50/mm^3, no more ATG-R was administered.
	  ○ If the T cell count was >50/mm^3, ATG-R was repeated at the same schedule and dose as the initial infusion.
	• Administration was planned for Days -5, -4, and -3 pre-implantation, followed by 2 days of rest prior to implantation.

Methylprednisolone[1,2]	• 2 mg/kg IV x 1 dose 4 hrs prior to ATG-R, then 0.5 mg/kg IV every 6 hrs until 24 hrs after the end of the ATG-R dosing
Cyclosporine[3,4,5]	• Target trough level of 180 to 220 ng/mL
Basiliximab	• A single dose of 5 mg/kg IV
MMF	• 15 mg/kg/dose q 8 hrs IV or PO
Alemtuzumab[6]	• 0.25 mg/kg daily, infused over 2 hours x 4 days IV

ATG-R: anti-thymocyte globulin [rabbit] (Thymoglobulin); IV: intravenous; MMF: mycophenolate mofetil; PO: oral.
[1]Additional pre-implantation corticosteroids (methylprednisolone) were used for atypical patients if pre-implantation CD3+ T cell numbers or the absolute lymphocyte count (ALC) was greater than 4,000 cells/mm^3. A starting dose of 1 mg/kg/day was used if the T cell count or ALC was between 4,000 and 10,000 cells/mm^3. A dose of 2 mg/kg/day was used if the T cell count was > 10,000 cells/mm^3.
[2] Corticosteroids (methylprednisolone or prednisolone) were initiated as soon as the diagnosis was confirmed in patients with evidence of maternal engraftment or with atypical cDGS and a PHA response of > 40,000 cpm on immunosuppression or > 75,000 cpm when not on immunosuppression. The steroid was weaned as soon as possible when the rash and other symptoms were brought under control.

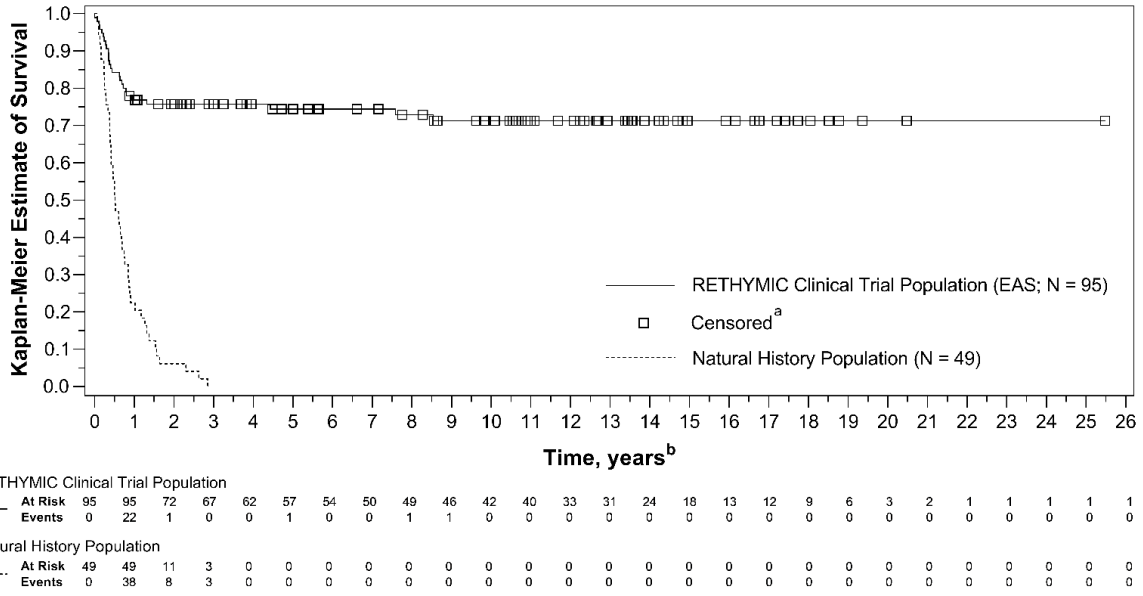
[3] Cyclosporine was initiated as soon as the diagnosis was confirmed and at least 7 days prior to ATG-R administration. If the CD3+ T cells fell and remained below 50/mm^3, cyclosporine was weaned to have a cyclosporine trough level of 100 to 150 ng/mL. If the T cell count remained over 50/mm^3, cyclosporine was maintained until the naive T cells were 10% of CD3+ T cells. Cyclosporine was then weaned over 10 weeks. To preserve renal function, the initiation of cyclosporine may have been delayed prior to implantation. Renal function was monitored according to the cyclosporine or tacrolimus prescribing information.
[4] A higher target trough concentration of 250 to 300 ng/mL was used in patients with evidence of maternal engraftment or with atypical cDGS and a PHA response of > 40,000 cpm on immunosuppression or > 75,000 cpm when not on immunosuppression.
[5] If the patient could not tolerate cyclosporine due to adverse events (AEs), then the immunosuppression could have been changed to tacrolimus (target trough concentration of 7 to 10 ng/mL). In patients with evidence of maternal engraftment or with atypical cDGS and a PHA response of > 40,000 cpm on immunosuppression or > 75,000 cpm when not on immunosuppression, the tacrolimus target trough level was 10 to 15 ng/mL.
6. Premedications given 30 minutes prior to alemtuzumab include methylprednisolone (1 mg/kg IV), acetaminophen (10 mg/kg IV), and diphenhydramine, (0.5 mg/kg IV).

The Kaplan-Meier estimated survival rates were 77% (95% CI [0.670, 0.841]) at 1 year and 76% (95% CI [0.658, 0.832]) at 2 years. For patients who were alive at 1 year after treatment with Rethymic, the survival rate was 94% at a median follow-up of 10.7 years.

Without treatment, CA is fatal in childhood. In a natural history population observed from 1991 through 2017, 49 patients diagnosed with congenital athymia received supportive care only. The 2-year survival rate was 6%, with all patients dying by 3 years of age. This population included 33 (67%) males. The most common cause of death was infection in 26 (53%) patients. Other common causes (≥10%) included support withdrawn in 7 (14%) patients, respiratory arrest in 5 (10%) patients, and cardiac arrest in 5 (10%) patients.

The Kaplan-Meier estimated survival rates for the Rethymic clinical trial population, and the natural history population are shown in Figure 1. Four patients with >50 naïve T cells/mm^3 (CD45RA+, CD62L+) at time of Rethymic administration have been treated; 2 (50%) were alive with follow-up less than 2 years.

Figure 1: Kaplan-Meier Survival by Year (RETHYMIC Efficacy Analysis Population and Natural History Population)



[a]Patients were censored at the time of their most recent follow-up for the RETHYMIC clinical trial program. No patients in the natural history population were censored.
[b]Time is years after administration for the RETHYMIC clinical trial population and years of life for the natural history population.

Rethymic significantly reduced the number of infections over time. In the first year after treatment with Rethymic, the number of patients with an infection event onset 6 to ≤ 12 months after treatment decreased by 38% (from 63 to 39) relative to the number of patients with an infection event onset in the first 6 months post-treatment. A two-year analysis showed a decrease in both the number of patients with an infection event and the mean number of infection events per patient, with an onset in the first 12 months post-treatment as compared to 12 to ≤ 24 months after treatment. There was a mean difference of 2.9 events ($p<0.001$) per patient.

Naïve CD4+ and CD8+ T cells reconstituted over the first year, with a durable increase through Year 2. Median (minimum, maximum) naïve CD4+ T cells/mm^3 increased from a baseline of 1 (0, 38) to values of 42 (0, 653), 212 (1, 751), and 275 (33, 858) at 6, 12, and 24 months after treatment with Rethymic, respectively. Median naïve CD8+ T cells/mm^3 increased from a baseline of 0 (0, 46) to values of 9 (0, 163), 58 (0, 304), and 86 (6, 275) at 6, 12, and 24 months after treatment with Rethymic, respectively. This was accompanied by functional improvements based on T cell proliferative responses to PHA.

Summary of Evidence

Congenital athymia is an ultra-rare condition in which children are born without a thymus, resulting in the inability to sufficiently fight infections. Rethymic (allogeneic processed thymus tissue-agdc) has been studied in 10 prospective, single-arm open-label trials from 1993-2020. Implanted into the quadriceps muscle, the use of Rethymic has supported the development of immunity in a patient's first year after receipt. After development of T cells, patients have demonstrated the ability to overcome serious infections. Based on this information, the U. S. Food and Drug Administration approved a Biologics License Application for Rethymic, which is

indicated for immune reconstitution in pediatric patients with congenital athymia. Therefore, Rethymic (allogeneic processed thymus tissue-agdc) may be considered medically necessary for immune reconstitution in pediatric patients with congenital athymia when criteria noted in coverage are met. Rethymic (allogeneic processed thymus tissue-agdc) is considered not medically necessary in patients with pre-existing cytomegalovirus infections or human immunodeficiency infections, or who have been previously treated with Rethymic. It is considered experimental, investigational and/or unproven for all other indications.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	C9399, J3490, J3590

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

References

1. FDA - Rethymic Highlights of Prescribing Information. Food and Drug Administration. (Revised 10/2021). Available at <http://accessdata.fda.gov> (accessed June 27, 2023).
2. National Organization for Rare Diseases. Complete DiGeorge Syndrome. (Updated Nov 1, 2021) Available at <http://www.rarediseases.org> (accessed June 27, 2023).
3. Collins C, Sharpe E, Silber A, et al. Congenital Athymia: Genetic Etiologies, Clinical Manifestations, Diagnosis, and Treatment. J Clin Immunol. Jul 2021; 41(5):881-895. PMID 33987750
4. FDA – October 8, 2021. Rethymic Summary Basis for Regulator Action. Food and Drug Administration. Available at <http://www. fda.gov> (accessed June 27, 2023).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <http://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
06/15/2024	Reviewed. No changes.
09/15/2023	Document updated with literature review. Coverage unchanged. References updated.
02/01/2023	Document updated. Coverage revised: Rethymic (allogeneic processed thymus tissue-agdc) may be considered medically necessary for immune reconstitution in pediatric patients ages 3 years or younger with congenital athymia when all of the following criteria are met: Patient has a diagnosis of congenital athymia confirmed by a pediatric immunologist; AND Patient does NOT have a diagnosis of severe combined immunodeficiency (SCID); AND Medical record documentation confirming the patient does NOT have pre-existing cytomegalovirus (CMV) infection OR human immunodeficiency virus (HIV) infection; AND Patient has not previously been treated with Rethymic; AND Diagnosis of congenital athymia has been confirmed with documentation of the following: Flow cytometry results demonstrating fewer than 50 naïve T-cells/mm3 (CD45RA+, CD62L+) in the peripheral blood or less than 5% of total T-cells being naïve in phenotype; AND One of the following: Genetic testing confirms 22q11.2 deletion; OR Hematopoietic stem cells (HSCs) successfully differentiate using artificial thymic organoid (ATO) system test; OR Patient has syndromic comorbidities (e.g., palatal anomalies, cardiac abnormalities, hypocalcemia, hearing loss, coloboma, etc.) associated with congenital athymia; AND Patient has documentation of screening for anti-HLA antibodies. Rethymic (allogeneic processed thymus tissue-agdc) is considered not medically necessary in patients with pre-existing cytomegalovirus (CMV) infection or human immunodeficiency (HIV) infection or have been previously treated with Rethymic. Dosing and Administration: The Rethymic implantation will not exceed a single, one-time dose (up to 22,000 mm2 of Rethymic surface area per m2 recipient BSA, not to exceed 42 slices) as calculated and supplied by the manufacturer. Rethymic (allogeneic processed thymus tissue-agdc) is considered experimental, investigational and/or unproven for all other indications. Title changed from Rethymic.
07/15/2022	Reviewed. No changes.
04/01/2022	New medical document. Rethymic (allogeneic processed thymus tissue-agdc) may be considered medically necessary for immune reconstitution in pediatric patients with congenital athymia. Rethymic is considered experimental, investigational and/or unproven for all other indications, including but not limited to, severe combined immunodeficiency (SCID).