# Clinical Policy: Allogenic Processed Thymus Tissue-agdc (Rethymic)

Reference Number: PA.CP.PHAR.563
Effective Date: 01/2023
Last Review Date: 01/2026

**Description**
Allogenic processed thymus tissue-agdc (Rethymic®) is a regenerative tissue-based therapy.

**FDA Approved Indication(s)**
Rethymic is indicated for immune reconstitution in pediatric patients with congenital athymia.

Limitation(s) of use: Rethymic is not indicated for the treatment of patients with severe combined immunodeficiency (SCID).

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness® that Rethymic is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Congenital Athymia** (must meet all)**:**

1. Diagnosis of congenital athymia;
2. Diagnosis is confirmed by $CD3^+$ $CD4^+$ $CD45RA^+$ $CD62L^+$ T-cell count < $50/mm^3$ or < 5% of the total T-cell count based on flow cytometry;
3. One of the following (a or b):
   a. Absence of genetic defects associated with SCID (*see Appendix E*);
   b. At least one of the following to define complete DiGeorge syndrome (cDGS): congenital heart defect, hypoparathyroidism/hypocalcemia, 22q11 hemizygosity, 10p13 hemizygosity, CHARGE syndrome (*see Appendix D*), or CHD7 mutation;
4. Prescribed by or in consultation with a pediatric immunologist;
5. Age ≤ 18 years;
6. Member does not have preexisting CMV infection (e.g., > 500 copies/mL in the blood by PCR on two consecutive assays), if member does have preexisting CMV infection the risks vs benefits were considered;
7. Documentation of anti-human leukocyte antigen (HLA) antibody screening prior to treatment;
8. If positive for anti-HLA antibodies, member must receive Rethymic from a donor who does not express HLA alleles;
9. If member previously received a hematopoietic cell transplantation (HCT) or a solid organ transplant, both of the following (a and b):
   a. HLA matching is required;
   b. Member must receive Rethymic HLA matched to recipient alleles that were not expressed in the HCT donor;

10. Rethymic is prescribed in combination with immunosuppressive therapy based on disease phenotype and phytohemagglutinin (PHA) levels *(see Appendix F)*;
11. Request meets both of the following (a and b);
    a. Dose does not exceed 22,000 $mm^2$ of Rethymic /$m^2$ recipient body surface area (up to 42 Rethymic slices);
    b. Request is for a one-time application only.

**Approval duration: 1 month (one time application only per lifetime)**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## II. Continued Therapy

**A. Congenital Athymia**

1. Continued therapy will not be authorized as Rethymic is indicated to be dosed one time only.

**Approval duration: Not applicable**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policies – PA.CP.PMN.53.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

ATG-R: anti-thymocyte globulin (rabbit)
cDGS: complete DiGeorge syndrome
CMV: cytomegalovirus
CPM: counts per minute
FDA: Food and Drug Administration
HCT: hematopoietic cell transplantation
HLA: human leukocyte antigens
MMF: mycophenylate mofetil
PCR: polymerase chain reaction
PHA: phytohemagglutinin
SCID: severe combined immunodeficiency

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

None reported

*Appendix D: General information*

- Congenital athymia is a rare condition characterized by the absence of a thymus at birth resulting in profound immunodeficiency and immune dysregulation. Children with congenital athymia generally do not survive beyond early childhood.
- CHARGE syndrome is a disorder that affects many areas of the body. CHARGE is an abbreviation for several of the features common in the disorder: coloboma, heart defects, atresia choanae (also known as choanal atresia), growth retardation, genital abnormalities, and ear abnormalities.

*Appendix E: SCID Defects*

| Disease | Genetic Defect |
|---|---|
| γc deficiency (X-linked SCID, CD132 deficiency | IL2RG |
| JAK3 deficiency | JAK3 |
| IL7Rα deficiency | IL7R |
| CD45 deficiency | PTPRC |
| CD3δ deficiency | CD3D |
| CD3ε deficiency | CD3E |
| CD3ζ deficiency | CD3Z |
| Coronin-1A deficiency | CORO1A |
| LAT deficiency | LAT |
| SLP76 deficiency | *LCP2* |
| RAG deficiency | RAG 1, RAG 2 |
| DCLRE1C (Artemis) deficiency | DCLRE1C |
| DNA PKcs deficiency | PRKDC |
| Cernunnos/XLF deficiency | NHEJ1 |
| DNA ligase IV deficiency | LIG4 |
| Adenosine deaminase (ADA) deficiency | ADA |
| AK2 defect | AK2 |
| Activated RAC2 defect | RAC2 |

*Appendix F: Treatment Assignment to Immunosuppression*

| Complete DiGeorge Anomaly Phenotype | PHA Response | Immunosuppression Used 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<br>Methylprednisolone |
| Typical | > 50,000 cpm | ATG-R<br>Methylprednisolone<br>Cyclosporine |
| Atypical | < 40,000 cpm on immunosuppression or < 75,000 cpm when not on immunosuppression | ATG-R<br>Methylprednisolone<br>Cyclosporine |

| Complete DiGeorge Anomaly Phenotype | PHA Response | Immunosuppression Used with Rethymic |
|---|---|---|
| Atypical | ≥40,000 cpm on immunosuppression or ≥75,000 cpm when not on immunosuppression or evidence of maternal engraftment | ATG-R<br>Methylprednisolone<br>Cyclosporine<br>Basiliximab<br>MMF |

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Congenital athymia | 5,000 to 22,000 $mm^2$ of Rethymic surface area per $m^2$ of recipient BSA as a single surgical procedure | 22,000 $mm^2$ of Rethymic surface area/$m^2$ recipient BSA; up to 42 cultured Rethymic slices |

## VI. Product Availability

Slices of processed tissue with varying thickness and shape; each drug product dish contains up to 4 Rethymic slices

## VII. References

1. Rethymic Prescribing Information. Cambridge, MA: Enzyvant Therapeutics, Inc; October 2024. Available at: https://www.rethymic.com/RETHYMIC_Prescribing_Information_English.pdf. Accessed October 23, 2025.
2. Collins C, Sharpe E, Silber A, Kulke S, Hsieh EWY. Congenital Athymia: Genetic Etiologies, Clinical Manifestations, Diagnosis, and Treatment. J Clin Immunol. 2021;41(5):881-895.
3. Markert ML, Gupton SE, McCarthy EA. Experience with cultured thymus tissue in 105 children [published online ahead of print, 2021 Aug 3]. J Allergy Clin Immunol. 2021;S0091-6749(21)01056-3. doi:10.1016/j.jaci.2021.06.028.
4. Tangye SG, Al-Herz W, Bousfiha A, et al. Human Inborn Errors of Immunity: 2022 Update on the Classification from the International Union of Immunological Societies Expert Committee. J Clin Immunol. 2022;42(7):1473-1507.

## Coding Implications

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.

| HCPCS Codes | Description |
|---|---|
| J3590 | Unclassified biologics |
| C9399 | Unclassified drugs or biologicals |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| Policy created | 01/2023 |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| 1Q 2024 annual review: no significant changes; references reviewed and updated. | 01/2024 |
| 1Q 2025 annual review: no significant changes; corrected "CDXH7" mutation to "CHD7"; references reviewed and updated. | 01/2025 |
| 1Q 2026 annual review: no significant changes; references reviewed and updated. | 01/2026 |