Rethymic® (allogeneic processed thymus tissue-agdc)
(Surgical Implant)

Document Number: IC-0648

Last Review Date: 01/04/2024
Date of Origin: 01/04/2022
Dates Reviewed: 01/2022, 01/2023, 01/2024

I. Length of Authorization

Coverage will be provided for 1 dose only

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Rethymic slices: Up to 42 slices (approximately 55,000 mm^2 of Rethymic)

B. Max Units (per dose and over time) [HCPCS Unit]:

- Up to 42 slices (approximately 55,000 mm^2) of Rethymic

III. Initial Approval Criteria

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

Congenital Athymia † Φ [1,3]

- Used for immune reconstitution in pediatric patients; **AND**
- Patient has a diagnosis of congenital athymia 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 *(Note: Requests for naïve T-cell counts ≥50 cells/mm^3 will be handled on a case-by-case basis)*; **AND**
    - Patient has athymia with a diagnosis of FOXN1 deficiency; **OR**
    - Patient has complete DiGeorge syndrome (cDGS), also referred to as complete DiGeorge anomaly (cDGA)**§**; **AND**
- Will not be used for the treatment of patients with severe combined immunodeficiency (SCID); **AND**
- Will not be used in patients with any of the following:

    - Heart surgery anticipated within 4 weeks prior to, or 3 months after, the planned Rethymic treatment date
    - Human immunodeficiency virus (HIV) infection
    - Deemed to be poor surgical candidates; **AND**
- Benefits and risks of treatment have been discussed with patients who have a pre-existing CMV infection or who have renal impairment; **AND**
- Patient has been screened for anti-HLA antibodies *(Note: Patients who have previously received a hematopoietic cell transplant with a mismatched allele require HLA matching of the thymus to that allele);* **AND**
- Patient will receive IVIG replacement and prophylactic antimicrobials prior to and after transplant until immune reconstitution (according to infection control protocols) occurs *(Note: Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with Rethymic)*; **AND**
- Patient will not receive live or inactivated vaccines until IVIG/immunosuppressive therapy is discontinued and immune reconstitution has occurred; **AND**
- Patients with elevated baseline T cell proliferative response to PHA ≥ 5,000 cpm or > 20-fold over background or have evidence of maternal engraftment will receive combination therapy with immunosuppressive agents (e.g., rabbit antithymocyte globulin with or without calcineurin inhibitors and/or steroids)

§ Definition of complete DiGeorge syndrome (cDGS) or complete DiGeorge anomaly (cDGA) [1,3]
Athymia plus 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 – CHD7 mutation

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage cannot be renewed.

V. Dosage/Administration [1]

Indication	Dose
Congenital Athymia	Administer in a single surgical session via implantation into a healthy bed of muscle tissue in one or both quadriceps muscles under general anesthesia. • The dosage is determined by the total surface area of the Rethymic slices and the recipient BSA. Rethymic slices are variable in size and shape and the dose of manufactured Rethymic will be calculated at the facility to correspond to the patient's calculated dose. The recommended dose range is 5,000 to 22,000 mm^2 of Rethymic/m^2 recipient BSA – up to 42 cultured Rethymic slices will be provided for each patient. • Immunosuppressive therapy is recommended for patients receiving Rethymic based on evidence of maternal engraftment or an elevated response to phytohemagglutinin (PHA) depending on phenotype. • Rethymic is surgically implanted at a single site in Durham, N.C.
– *Store at room temperature in the polycarbonate container in the insulated shipping box until ready for use. Do not refrigerate, freeze, agitate, or attempt to sterilize.* – *Manufacturing personnel record which slices are used during the surgery. If any slices are not administered to the patient, manufacturing personnel return this tissue to the manufacturing facility and dispose of this tissue as biohazardous waste in accordance with local requirements. Manufacturing personnel calculate the total dose that was administered to the patient.* – *Use Rethymic prior to the time and date of expiration printed on the polycarbonate container.* – *Monitoring parameters include, but are not limited to, phytohemagglutinin (PHA) response, CD3+ naïve T-cells, CD4+ T-cell count, IgG trough, infections, GvHD, & autoimmune disorders.*	

VI. Billing Code/Availability Information

HCPCS code:

- J3590 – Unclassified biologics
- C9399 – Unclassified drugs or biologicals

NDC(s):

- Rethymic single-dose unit supplied with up to forty-two ready-to-use slices of processed thymus tissue: 72359-0001-xx

VII. References

1. Rethymic [package insert]. Marlborough, MA; Sumitomo Pharma America, Inc.; July 2023. Accessed December 2023.
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. doi.org/10.1007/s10875-021-01059-7.
3. Markert ML, Gupton SE, McCarthy EA. Experience with cultured thymus tissue in 105 children. J Allergy Clin Immunol. Published online August 3, 2021. doi:10.1016/j.jaci.2021.06.028

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D82.1	Di George's Syndrome
D82.8	Immunodeficiency associated with other specified major defects

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC