Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 02/13/2025

Rethymic® (allogenic processed thymus tissue – agdc)

HCPCS: J3490

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Member does not have severe combined immunodeficiency (SCID)
   d. The requesting physician attests to providing clinical outcome information within the appropriate provider portal as requested by BCBSM.
   e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Six months
   c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Rethymic is indicated for immune reconstitution in pediatric patients with congenital athymia.
    - Limitation of use: Rethymic is not indicated for the treatment of patients with SCID.
- The use of Rethymic involves the migration of recipient T cell progenitors from the bone marrow to implanted Rethymic slices, where they develop into naïve immunocompetent recipient T calls. Evidence of thymic function can

be observed with the development of naïve T cells in the peripheral blood; this is unlikely to be observed prior to 6-12 months after treatment with Rethymic.

- Congenital athymia is an ultra-rare immune disorder in which a child is born without a thymus. Infants born without a thymus have profound immunodeficiency, and without treatment, many die from infections or autoimmune symptoms by 2 or 3 years of age. The exact incidence or prevalence of congenital athymia is unknown, but the condition affects boys and girls. About 17-24 infants per 4 million in the United States are born with congenital athymia.

- Congenital athymia is sometimes mistaken for SCID; patients with either disorder present with very low T-cell counts. Both congenital athymia and SCID are primary immunodeficiency disorders, but they are 2 separate conditions. SCID is caused by a dysfunction of hematopoietic stem cells of the bone marrow, whereas congenital athymia is associated with a dysfunction or absence of the thymus.

- Congenital athymia often occurs in babies who have certain genetic problems, especially DiGeorge syndrome (DGS, sometimes referred to as 22q11.2 deletion syndrome). Congenital athymia is often associated with other conditions, including coloboma, heart defects, atresia choanae, retardation of growth and development, genital hypoplasia, and ear anomalies/deafness (CHARGE syndrome), as well as forkhead box protein N1 (FOXN1) deficiency. Nongenetic, environmental factors (i.e. maternal diabetes; exposure to alcohol, retinoids, or bis-dichloroacetylamine) have also been associated with congenital athymia. Originally, the term congenital athymia was used interchangeably with complete DiGeorge anomaly or DiGeorge syndrome(cDGS), but current research shows that there are distinct genetic and nongenetic conditions associated with congenital athymia.

- In the 10 prospective, single-center, open-label studies that enrolled 105 patients to evaluate the efficacy of Rethymic, the diagnosis of congenital athymia was based on flow cytometry documenting 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.

- Per the American Academy of Allergy, Asthma & Immunology (AAAAI; 2017), management of patients with congenital athymia focuses on supportive care to reduce the risk of infection until the underlying immune deficiency can be corrected. Similar to other primary immunodeficiencies, as soon as congenital athymia is suspected afterbirth, it is recommended that neonates in the hospital be placed in reverse isolation with air filtering systems (HEPA, LAF).

- In addition to isolation, patients with congenital athymia should begin antimicrobial prophylaxis to prevent bacterial, viral and fungal infections.

- B-cell function is usually reduced in these patients, so they should receive immunoglobulin replacement. Human immunoglobulin preparations for intravenous or subcutaneous administration are the cornerstone of treatment in patients with primary immunodeficiency diseases affecting the humoral immune system. Given the potential risks and inherent scarcity of human immunoglobulin, careful consideration of its indications and administration is warranted.

- Hematopoietic stem cell transplant (HSCT) has been performed in congenital athymia patients with relatively little success. Survival after HSCT is low and significant adverse events have been reported in athymic patients, including graft versus host disease in ~50% of patients. Immune reconstitution in athymic patients post-HSCT is also poor with no clear evidence of successful regeneration of naïve T cells.

References:

1. Rethymic [package insert]. Cambridge, MA: Enzyvant Therapeutics, Inc. October 2021.
2. FDA approves innovative treatment for pediatric patients with congenital athymia. News release. US Food and Drug Administration. Accessed November 20, 2021.https://www.fda.gov/news-events/press-announcements/fda-approves-innovative-treatment-pediatric-patients-congenital-athymia.
3. Enzyvant receives FDA approval for Rethymic®(allogeneic processed thymus tissue-agdc), a one-time regenerative tissue-based therapy for pediatric congenital athymia. News release. Enzyvant Therapeutics, Inc. Accessed November 20, 2021.https://www.globenewswire.com/news-release/2021/10/09/2311432/0/en/Enzyvant-Receives-FDA-Approval-for-RETHYMIC-allogeneic-processed-thymus-tissue-agdc-a-One-Time-Regenerative-Tissue-Based-Therapy-for-Pediatric-Congenital-Athymia.html
4. Perez EE, Orange JS, Bonilla F, Chinen J, Chinn IK, Dorsey M, El-Gamal Y, Harville TO, Hossny E, Mazer B, Nelson R, Secord E, Jordan SC, Stiehm ER, Vo AA, Ballow M. Update on the use of immunoglobulin in human disease: Areview of evidence. J Allergy Clin Immunol.2017 Mar;139(3S):S1-S46. doi: 10.1016/j.jaci.2016.09.023. Epub 2016 Dec 29. PMID: 28041678.
5. 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:10.1007/s10875-021-01059-7
6. Congenital athymia: Information for healthcare professionals. Healthcare professional brochure. Athymia Insights. Accessed October 18, 2021. https://www.athymiainsights.com/wp-content/themes/athymia-insights/assets/pdfs/HCP_Disease_state_Brochure_2_19_2020.pdf
7. IPD Analytics. New Drug Approval Review: Rethymic for the Treatment of Congenital Athymia. October20, 2021. Accessed November 20, 2021. https://www.ipdanalytics.com

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.4</td><td>Effective Date: 02/13/2025</td><td>Updated criteria to include outcomes tracking requirement for cellular therapies</td></tr>
<tr><td>1.3</td><td>Effective Date: 02/08/2024</td><td>Annual review of criteria was performed. No changes were made.</td></tr>
<tr><td>1.2</td><td>Effective Date: 11/16/2023</td><td>UM medical management system update for BCBSM and BCN
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<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>No</td></tr>
<tr><td>BCNA</td><td>No</td></tr>
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<tr><td>1.1</td><td>Effective Date: 02/02/2023</td><td>Annual review of criteria was performed. No changes were made.</td></tr>
<tr><td>1.0</td><td>Effective Date: 02/10/2022</td><td>New policy
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form

Blue Cross Blue Shield Blue Care Network of Michigan

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This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
3. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
   ☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
4. Please specify location of administration if hospital outpatient infusion: _____
5. Please specify location of administration if hospital inpatient infusion: _____
6. Please provide the NPI number for the place of administration: _____
7. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis? _____
   b. What other medication has the patient received for their condition? Please list_____
      i. Please describe the response to previous therapies:
      _____
   c. Will the patient be receiving any other treatment for the listed condition while on this medication? Please list:
      _____
   d. Please list any labs values important for diagnosing or monitoring this patient's condition:
      _____
8. **Continuation of therapy:**
   a. Has the patient progressed while on this medication? ☐ yes ☐ no
   b. How has the patient's condition changed while on this medication?
      ☐ Improved: Please describe: _____
      ☐ Stable: please describe: _____
      ☐ Worsened; Please describe: _____
      ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review **(required)**

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021