INDICATION
RETHYMIC® (allogeneic processed thymus tissue–agdc) is indicated for immune reconstitution in pediatric patients with congenital athymia.

Limitations of Use: RETHYMIC is not indicated for the treatment of patients with severe combined immunodeficiency (SCID).

FDA APPROVAL
RETHYMIC was approved by the US Food and Drug Administration (FDA) on October 8, 2021.

NATIONAL DRUG CODE (NDC) FOR RETHYMIC

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>NDC 72359-001-01</td>
<td>Single-dose unit, consists of yellow to brown slices of allogeneic processed thymus tissue for administration by surgical implantation. Three to 11 drug product containers, with a total of 10 to 42 RETHYMIC slices, are provided for each patient. Each drug product container provides up to 4 RETHYMIC slices of variable size.</td>
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DESCRIPTION
RETHYMIC is an allogeneic processed thymus tissue product for administration by surgical implantation. Thymus tissue is obtained from donors less than or equal to 9 months of age undergoing cardiac surgery. This thymus tissue is aseptically processed and cultured for 12 to 21 days to produce RETHYMIC. The manufacturing process preserves the thymic epithelial cells and tissue structure and depletes most of the donor thymocytes from the tissue. RETHYMIC is then surgically implanted into patients with congenital athymia.

MECHANISM OF ACTION
RETHYMIC is intended to reconstitute immunity in patients who are athymic. The proposed mechanism of action involves the migration of recipient T cell progenitors from the bone marrow stem cells to the implanted RETHYMIC slices, where they develop into naive immunocompetent recipient T cells. Evidence of thymic function can be observed with the development of naive T cells in the peripheral blood; this is unlikely to be observed prior to 6 to 12 months after treatment with RETHYMIC.

DOSEAGE
RETHYMIC is administered by a surgical procedure. The dosage is determined by the total surface area of the RETHYMIC slices and the 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 mm² of RETHYMIC surface area/m² recipient BSA. At the time of surgery, the manufacturing personnel communicate to the surgical team the portion of the product that represents the minimum dose. Please see the RETHYMIC Prescribing Information for additional dosage information.

HOW SUPPLIED
RETHYMIC is supplied as a single-dose unit of ready-for-use slices of processed thymus tissue, in sterile, polystyrene dishes (drug product dishes). Each drug product dish contains up to 4 RETHYMIC slices, adhered to circular filter membranes on top of surgical sponges in 5 mL of medium containing fetal bovine serum. A total of 10 to 42 RETHYMIC slices are supplied according to the dosage calculated in advance by the manufacturer for the specific patient. All drug product dishes are supplied in a polycarbonate container in an insulated shipping box.

SUGGESTED BILLING CODE*

| ICD-10-CM | D82.1 Di George’s Syndrome |

ICD-10-CM = International Classification of Diseases, Tenth Revision, Clinical Modification.

*This code is not all-inclusive. Appropriate codes vary by patient, payer, and setting for care. Correct coding is the responsibility of the provider submitting the claim.

AVAILABILITY
Duke Health, located in Durham, NC, is the single site of care for surgical implantation of RETHYMIC.

Important Safety Information

Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with RETHYMIC. Given the immunocompromised condition of athymic patients, follow infection control measures until the development of thymic function is established as measured through flow cytometry. Monitor patients closely for signs of infection including fever.
Important Safety Information (cont.)

If a fever develops, assess the patient by blood and other cultures and treat with antimicrobials as clinically indicated. Patients should be maintained on immunoglobulin replacement therapy until specified criteria are met, and two months after stopping, IgG trough level should be checked. Prior to and after treatment with RETHYMIC, patients should be maintained on *Pneumocystis jiroveci* pneumonia prophylaxis until specified criteria are met.

RETHYMIC may cause or exacerbate pre-existing graft versus host disease (GVHD). Monitor and treat patients at risk for the development of GVHD. Risk factors for GVHD include atypical complete DiGeorge anomaly phenotype, prior hematopoietic cell transplantation (HCT) and maternal engraftment. GVHD may manifest as fever, rash, lymphadenopathy, elevated bilirubin and liver enzymes, enteritis, and/or diarrhea.

Autoimmune-related adverse events occurred in patients treated with RETHYMIC. These events included: thrombocytopenia, neutropenia, proteinuria, hemolytic anemia, alopecia, hypothyroidism, autoimmune hepatitis, autoimmune arthritis, transverse myelitis, albinism, hyperthyroidism, and ovarian failure. Monitor for the development of autoimmune disorders, including complete blood counts with differential, liver enzymes, serum creatinine, urinalysis, and thyroid function.

Pre-existing renal impairment is a risk factor for death.

In the clinical studies of RETHYMIC, 3 out of 4 patients with pre-existing cytomegalovirus infection died. The benefits/risks of treatment should be considered prior to treating patients with pre-existing CMV infection.

Because of the underlying immune deficiency, patients who receive RETHYMIC may be at risk of developing post-treatment lymphoproliferative disorder. Patients should be monitored for the development of lymphoproliferative disorder.

Transmission of infectious disease may occur because RETHYMIC is derived from human tissue and because product manufacturing includes porcine- and bovine-derived reagents.

Immunizations should not be administered in patients who have received RETHYMIC until immune-function criteria have been met.

All patients should be screened for anti-HLA antibodies prior to receiving RETHYMIC. Patients testing positive for anti-HLA antibodies should receive RETHYMIC from a donor who does not express those HLA alleles. HLA matching is required in patients who have received a prior HCT or a solid organ transplant. Patients who have received a prior HCT are at increased risk of developing GVHD after RETHYMIC if the HCT donor did not fully match the recipient.

Of the 105 patients in clinical studies, 29 patients died, including 23 deaths in the first year (< 365 days) after implantation.

The most common (>10%) adverse events related to RETHYMIC included: hypertension, cytokine release syndrome, rash, hypomagnesemia, renal impairment/failure, thrombocytopenia, and graft versus host disease.

To report suspected adverse reactions, please contact the FDA at 1-800-FDA-1088 or [www.fda.gov/safety/medwatch](http://www.fda.gov/safety/medwatch).

Please see full Prescribing Information at [RETHYMIC.com](http://RETHYMIC.com).