RETHYMIC®
allogeneic processed thymus tissue-agdc

HELP YOUR CHILD WITH CONGENITAL ATHYMIA

Discover the wonder of childhood

RETHYMIC is the first and only FDA-approved tissue-based treatment for congenital athymia. It is engineered to help children develop an immune system sufficient to fight infections.[1,2]

Indication

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

RETHYMIC is not for use in patients who have been diagnosed with severe combined immunodeficiency (SCID).

Important Safety Information

Infection Control: Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with RETHYMIC. Immune reconstitution is needed for the body to produce cells in the immune system to fight infection. Your child's doctor should advise you of infection control measures which should be followed immediately after treatment and until the immune system starts working at a sufficient level. Monitor your child closely for signs of infection, including fever. Your child should be maintained on immunoglobulin replacement and prophylactic antimicrobials until certain criteria are met as determined by your doctor.

Please see additional Important Safety Information and the QR code to the full Prescribing Information on pages 10 & 11, or visit RETHYMIC.com/prescribing-information.

Jada, a child with congenital athymia.

Scan the QR code to learn about our patient support program, or visit EnzyvantCONNECT.com

What is RETHYMIC?

RETHYMIC is the first and only treatment for congenital athymia[1,2]

RETHYMIC is an FDA-approved tissue-based treatment for congenital athymia. It is engineered to help children develop an immune system sufficient to fight infections.[1,2]

Important Safety Information (cont'd)

Graft versus Host Disease (GVHD): RETHYMIC may cause or make pre-existing GVHD worse. Your child will be monitored for GVHD and treated if needed. Symptoms of GVHD may include fever, rash, enlarged lymph nodes, inflammation of the gastrointestinal system and/or diarrhea.

RETHYMIC®
allogeneic processed thymus tissue-agdc

RETHYMIC is a one-time treatment administered via a single surgical procedure[1,2]

RETHYMIC is implanted in one, or both if necessary, of the thighs of a child with congenital athymia. The thigh muscle is used because its rich supply of blood provides oxygen and nutrients to RETHYMIC. After it is implanted, it is believed that the child's pre-T cells migrate to RETHYMIC where they develop into T cells that are sufficient to fight infections.[1,3]

What is congenital athymia?

Congenital athymia is a rare immune condition that requires children and often their families to live in strict isolation due to a lack of a functioning immune system.[4]

Children with congenital athymia are born without a thymus. The thymus is an organ that sits on top of the heart and plays an important role in how the immune system works.[5]

Important Safety Information (cont'd)

Autoimmune Disorders: Autoimmune-related adverse events occurred in patients treated with RETHYMIC. These events included: low platelets, low white blood cells, protein in urine, low red blood cells, hair loss, poor thyroid function, inflammation of liver, inflammation of the joints, inflammation of the spinal cord, loss of pigment in the skin, eyes and hair, overactive thyroid function, and loss of function of the ovaries. Your doctor will monitor your child regularly including performing blood tests.

Please see additional Important Safety Information and the QR code to the full Prescribing Information on pages 10 & 11, or visit RETHYMIC.com/prescribing-information.

Not actual patients.

How is RETHYMIC made?

Unlike a transplant, RETHYMIC is developed for one child at a time through a complex process using donor thymus tissue[1,6]

Donation

When an infant less than 9 months of age has cardiac surgery, some thymus tissue may need to be removed to access the heart. With consent of the infant donor's parents or guardian, **the thymus tissue is donated to make RETHYMIC.[6]**

Unlike many other medications, RETHYMIC is not an off-the-shelf product. **The tissue from a single pediatric donor allows for the manufacturing of RETHYMIC for one child.[1]**

The availability of RETHYMIC is dependent on multiple factors, including the size of the thymus tissue that is donated.[7]

Development

The amount of time the engineering process takes depends on multiple factors and can be completed between **12 and 21 days.[7]**

During this 12- to 21-day engineering process, most of the donor's pre-T cells are removed and **the tissue is tested repeatedly to ensure the product meets FDA safety standards.** Through this process, the donor thymus tissue becomes the FDA-approved treatment, RETHYMIC.[1,7]

Implantation

The available dosage is based on the donor thymus tissue, and the amount implanted is based on the recipient's body surface area.[1]

Once released from the manufacturing facility, **RETHYMIC must be implanted within a limited time frame at the treatment center.[7]**

The manufacturing of RETHYMIC must be carefully coordinated with the preparation of a potential recipient.[7]

Brynlee, a child with congenital athymia.

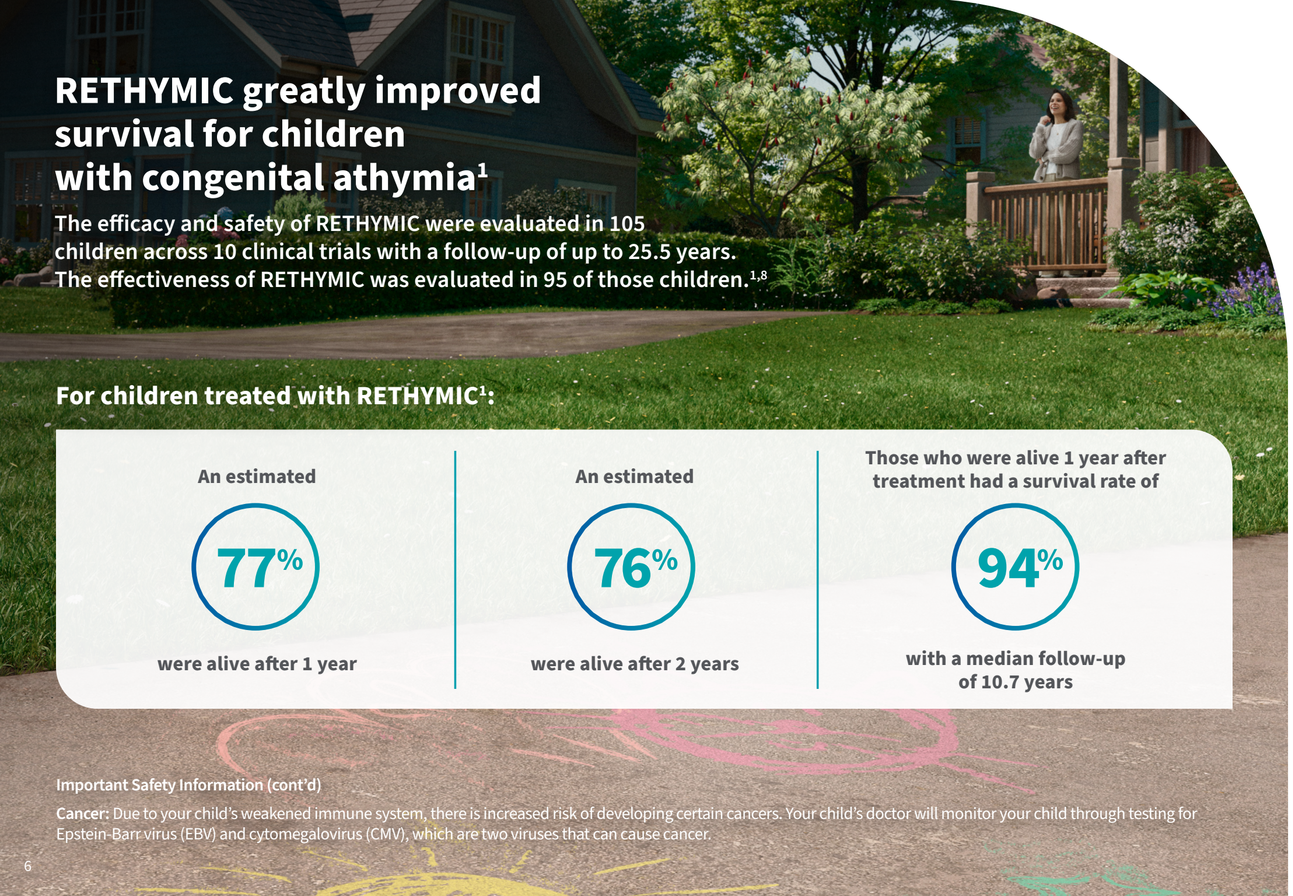
Important Safety Information (cont'd)

Kidney Disease: Treatment with RETHYMIC is a risk factor for death in patients with pre-existing kidney disease.

Important Safety Information (cont'd)

Cytomegalovirus (CMV) Infection: In clinical studies with RETHYMIC, 4 out of 4 patients with pre-existing CMV infection prior to the implantation with RETHYMIC died. Talk to your doctor about the benefits/risks of treatment if your child has pre-existing CMV infection.

Please see additional Important Safety Information and the QR code to the full Prescribing Information on pages 10 & 11, or visit RETHYMIC.com/prescribing-information.



RETHYMIC greatly improved survival for children with congenital athymia[1]

The efficacy and safety of RETHYMIC were evaluated in 105 children across 10 clinical trials with a follow-up of up to 25.5 years. The effectiveness of RETHYMIC was evaluated in 95 of those children.[1,8]

For children treated with RETHYMIC[1]:

An estimated **77%** were alive after 1 year

An estimated **76%** were alive after 2 years

Those who were alive 1 year after treatment had a survival rate of **94%** with a median follow-up of 10.7 years

Important Safety Information (cont'd)

Cancer: Due to your child's weakened immune system, there is increased risk of developing certain cancers. Your child's doctor will monitor your child through testing for Epstein-Barr virus (EBV) and cytomegalovirus (CMV), which are two viruses that can cause cancer.

RETHYMIC®
allogeneic processed thymus tissue-agdc

RETHYMIC significantly reduced the number of infections over time[1]:

38% **fewer children experienced an infection between 6 and 12 months after treatment with RETHYMIC vs the first 6 months after treatment**

In a 2-year analysis, fewer children experienced an infection and the average number of infections per child decreased in the second year after treatment.

The safety of RETHYMIC was demonstrated in 105 children across 10 clinical trials[1]

The most common side effects of RETHYMIC were[1,5]:

- Hypertension (high blood pressure)
- Cytokine release syndrome (overactive immune system)
- Hypomagnesemia (low magnesium)
- Rash
- Renal impairment/failure (decrease of kidney function)
- Thrombocytopenia (low platelets)
- Graft versus host disease (a condition in which a person's T cells attack their own body)

Of the 105 children in clinical studies, 29 died. The majority of deaths in the first year after receiving RETHYMIC were due to infections.[1]

Important Safety Information (cont'd)

Transmission of Serious Infections: Because RETHYMIC is made from human tissue, and animal products are used in the manufacturing process, transmission of infectious diseases may occur.

Please see additional Important Safety Information and the QR code to the full Prescribing Information on pages 10 & 11, or visit RETHYMIC.com/prescribing-information.

The treatment journey

RETHYMIC is currently only available at Duke University Health System in Durham, North Carolina[4]

Your child's healthcare provider will need to reach out to Duke University Health System to begin the process of referring them for RETHYMIC.

Consider speaking to your child's healthcare provider about enrolling in Enzyvant CONNECT® while they start the referral process.

Sumitomo Pharma America, Inc. and Enzyvant CONNECT are not responsible for treatment decisions or timing for treatment.

Important Safety Information (cont'd)

Vaccinations: Your child should not receive any vaccinations until he or she has met certain requirements set by your doctor. Talk to your child's doctor prior to any vaccinations.

Brynlee, a child with congenital athymia.

RETHYMIC®
allogeneic processed thymus tissue-agdc

Proper post-treatment care is critical to protect your child[1]

RETHYMIC needs time to help develop an immune system sufficient to protect from infections, which is unlikely to develop prior to 6 to 12 months after treatment. For some children, it may take up to 2 years.[1]

Your child will remain immune compromised while RETHYMIC starts to work, so to keep them safe, life immediately after treatment will have to look very similar to life before it. Careful monitoring and isolation are required to ensure your child avoids infection and other complications after treatment.[1,3,5]

Work with your child's healthcare provider to determine when infection prevention measures can be lifted.

Important Safety Information (cont'd)

Anti-HLA Antibodies: Prior to receiving RETHYMIC your child will be tested for HLA antibodies, which are proteins that may be present in your child's blood. If your child has these antibodies, he/she will need to receive RETHYMIC from a donor that does not express those HLA proteins.

Please see additional Important Safety Information and the QR code to the full Prescribing Information on pages 10 & 11, or visit RETHYMIC.com/prescribing-information.

Indication

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

RETHYMIC is not for use in patients who have been diagnosed with severe combined immunodeficiency (SCID).

Important Safety Information

Infection Control: Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with RETHYMIC. Immune reconstitution is needed for the body to produce cells in the immune system to fight infection. Your child's doctor should advise you of infection control measures which should be followed immediately after treatment and until the immune system starts working at a sufficient level. Monitor your child closely for signs of infection, including fever. Your child should be maintained on immunoglobulin replacement and prophylactic antimicrobials until certain criteria are met as determined by your doctor.

Graft versus Host Disease (GVHD): RETHYMIC may cause or make pre-existing GVHD worse. Your child will be monitored for GVHD and treated if needed. Symptoms of GVHD may include fever, rash, enlarged lymph nodes, inflammation of the gastrointestinal system and/or diarrhea.

Autoimmune Disorders: Autoimmune-related adverse events occurred in patients treated with RETHYMIC. These events included: low platelets, low white blood cells, protein in urine, low red blood cells, hair loss, poor thyroid function, inflammation of liver, inflammation of the joints, inflammation of the spinal cord, loss of pigment in the skin, eyes and hair, overactive thyroid function, and loss of function of the ovaries. Your doctor will monitor your child regularly including performing blood tests.

Kidney Disease: Treatment with RETHYMIC is a risk factor for death in patients with pre-existing kidney disease.

Cytomegalovirus (CMV) Infection: In clinical studies with RETHYMIC, 4 out of 4 patients with pre-existing CMV infection prior to the implantation with RETHYMIC died. Talk to your doctor about the benefits/risks of treatment if your child has pre-existing CMV infection.

Cancer: Due to your child's weakened immune system, there is increased risk of developing certain cancers. Your child's doctor will monitor your child through testing for Epstein-Barr virus (EBV) and cytomegalovirus (CMV), which are two viruses that can cause cancer.

Transmission of Serious Infections: Because RETHYMIC is made from human tissue, and animal products are used in the manufacturing process, transmission of infectious diseases may occur.

Vaccinations: Your child should not receive any vaccinations until he or she has met certain requirements set by your doctor. Talk to your child's doctor prior to any vaccinations.

Anti-HLA Antibodies: Prior to receiving RETHYMIC your child will be tested for HLA antibodies, which are proteins that may be present in your child's blood. If your child has these antibodies, he/she will need to receive RETHYMIC from a donor that does not express those HLA proteins.

RETHYMIC®
allogeneic processed
thymus tissue-agdc

Important Safety Information (cont'd)

HLA Typing: If your child has received a hematopoietic cell transplantation (HCT) or a solid organ transplant, they will have a test to look for specific antibodies that could interfere with the effect of RETHYMIC. If they are present, then it will be necessary to receive RETHYMIC from a certain group of donors that do not have these proteins.

Deaths: 105 children participated in the clinical studies of RETHYMIC. 29 of the patients died, including 23 in the first year after implantation of RETHYMIC.

What are the most common side effects with RETHYMIC?

The most common side effects with RETHYMIC are hypertension (high blood pressure), cytokine release syndrome, rash, hypomagnesemia (low magnesium), renal impairment / failure (decrease of kidney function), thrombocytopenia (low platelets), and graft versus host disease.

These are not all of the possible side effects of RETHYMIC. Talk to your child's doctor about any side effect that bothers your child or does not go away.

You are encouraged to report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/safety/medwatch.

References:

1. RETHYMIC [package insert]. Marlborough, MA: Sumitomo Pharma America, Inc; 2023. **2.** Enzyvant Therapeutics GmbH. Enzyvant receives FDA approval for RETHYMIC® (allogeneic processed thymus tissue-agdc), a one-time regenerative tissue-based therapy for pediatric congenital athymia. Enzyvant Therapeutics, Inc. October 8, 2021. Accessed March 3, 2023. https://enzyvant.com/enzyvant-receives-fda-approval-for-rethymic-allogeneic-processed-thymus-tissue-agdc-a-one-time-regenerative-tissue-based-therapy-for-pediatric-congenital-athymia/ **3.** Gupton SE, McCarthy EA, Markert ML. Care of children with DiGeorge before and after cultured thymus tissue implantation. *J Clin Immunol.* 2021;41(5):896-905. doi:10.1007/s10875-021-01044-0 **4.** Hsieh EWY, Kim-Chang JJ, Kulke S, Silber A, O'Hara M, Collins C. Defining the clinical, emotional, social, and financial burden of congenital athymia. *Adv Ther.* 2021;38(8):4271-4288. doi:10.1007/s12325-021-01820-9 **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.** Markert ML. Defects in thymic development. In: Sullivan KE, Stiehm ER, eds. *Stiehm's Immune Deficiencies: Inborn Errors of Immunity.* 2nd ed. Elsevier; 2020:1229-1239. **7.** Food and Drug Administration. Summary Basis for Regulatory Action. October 8, 2021. BLA STN: 125685/0. **8.** Markert ML, Gupton SE, McCarthy EA. Experience with cultured thymus tissue in 105 children. *J Allergy Clin Immunol.* 2022;149(2):747-757. doi:10.1016/j.jaci.2021.06.028

Please scan the QR code to see the full Prescribing Information, or visit RETHYMIC.com/prescribing-information

Supporting children and their families

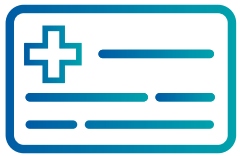
Enrolling in the Enzyvant CONNECT® Patient Support Program will give you and your family access to **educational resources** and, if eligible, **financial assistance** as you navigate the congenital athymia journey. Enzyvant CONNECT is available to patients with any type of insurance—including commercial plans, Medicare, or Medicaid—as well as patients who are underinsured or have no insurance coverage.

Dedicated care team

- Your Support Liaison will help you understand your child's diagnosis
- Your Access Specialist can help you navigate insurance benefits and financial assistance

Access to exclusive resources

- Document organizer
- *Sadie's Search*, a storybook written specifically with your child in mind
- Interactive T-cell progress tracker
- Activity book
- And more!



Co-pay program

- The Enzyvant CONNECT® Commercial Co-Pay Program can help caregivers of eligible commercially-insured patients in the US and US territories
- You may receive co-pay assistance for medication-related out-of-pocket costs for a treatment for congenital athymia

Scan the QR code to start your enrollment, or visit EnzyvantCONNECT.com/get-started

Call 844-ENZCNCT (844-369-2628) to get connected to personalized support.
Support is available Monday–Friday, 8:00 AM to 8:00 PM ET.

Sumitomo Pharma