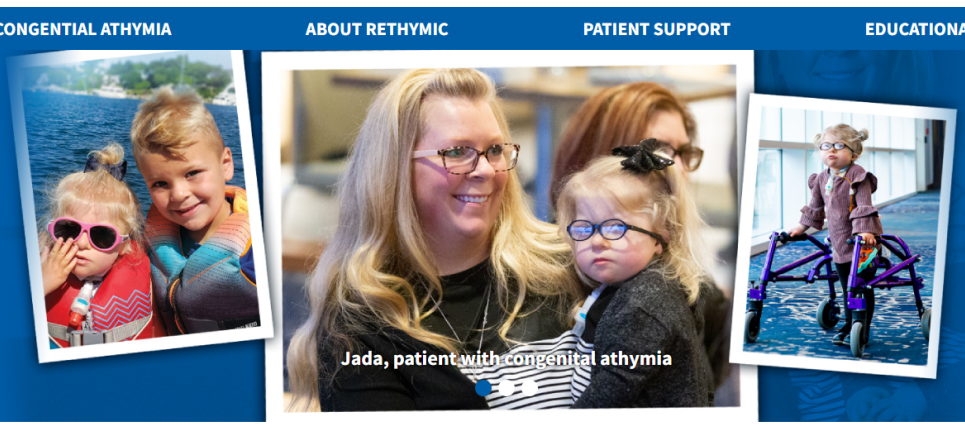

About Congenital Athymia

Congenital athymia is an ultra-rare immune condition in which a child is born without a thymus.

LEARN MORE

About RETHYMIC® (allogeneic processed thymus tissue–agdc)

Find information about the RETHYMIC efficacy and safety profile.

LEARN MORE

Patient Support

Enzyvant CONNECT is here to provide personalized support to patients and caregivers with congenital athymia.

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LEARN MORE

Educational Resources

Find information, downloads, links to medical literature and patient organizations.

LEARN MORE

ENZYVANT CONNECT

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Not an actual patient.

Indication and Important Safety Information

IMPORTANT SAFETY INFORMATION

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REFERENCES

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About Congenital Athymia

Learn about the diagnostic pathway for congenital athymia, including how to differentiate it from severe combined immunodeficiency (SCID), and about the different phenotypes of congenital athymia.

What is congenital athymia?

Congenital athymia is an ultra-rare immune condition primary immunodeficiency which is characterized by the lack of a functional thymus at birth. Estimated incidence in the United States is approximately 17 to 24 infants for every 4 million. Congenital athymia results in profound immunodeficiency and immune dysregulation[1,3]. The clinical manifestations are a direct result of the absence of the thymus and the inability to produce immunocompetent T-cells, leading to increased susceptibility to infection. These infections and autoimmune conditions can be fatal, and with only supportive care, children with congenital athymia typically do not survive beyond 2 to 3 years of age[4].

The thymus

The thymus is the only organ where thymocytes can mature, be selected, and ultimately survive to become naïve T-cells. Although T-cells originate in the bone marrow as progenitor cells, the bone marrow is not equipped with specialized tissue required for T-cell maturation[1]. T-cell progenitors emerging from the bone marrow migrate to the thymus for maturation, where they are selected to become naïve T-cells via positive and negative selection. Some progenitor cells begin to express CD4 or CD8 receptors. Subsequent downregulation of CD4 or CD8 results in development of naïve single positive cells that can exit the thymus and enter the peripheral bloodstream[1].

What conditions are associated with congenital athymia?

Congenital athymia may be associated with other conditions such as: DiGeorge syndrome (22q11.2 deletion syndrome); mutations in the genes TBX1, CHD7, (CHARGE syndrome), and FOXN1 (FOXN1 deficiency); diabetic embryopathy[1, 3, 6]. These multi-faceted conditions and syndromes make the already complex diagnosis of congenital athymia even more challenging.

Newborn screening

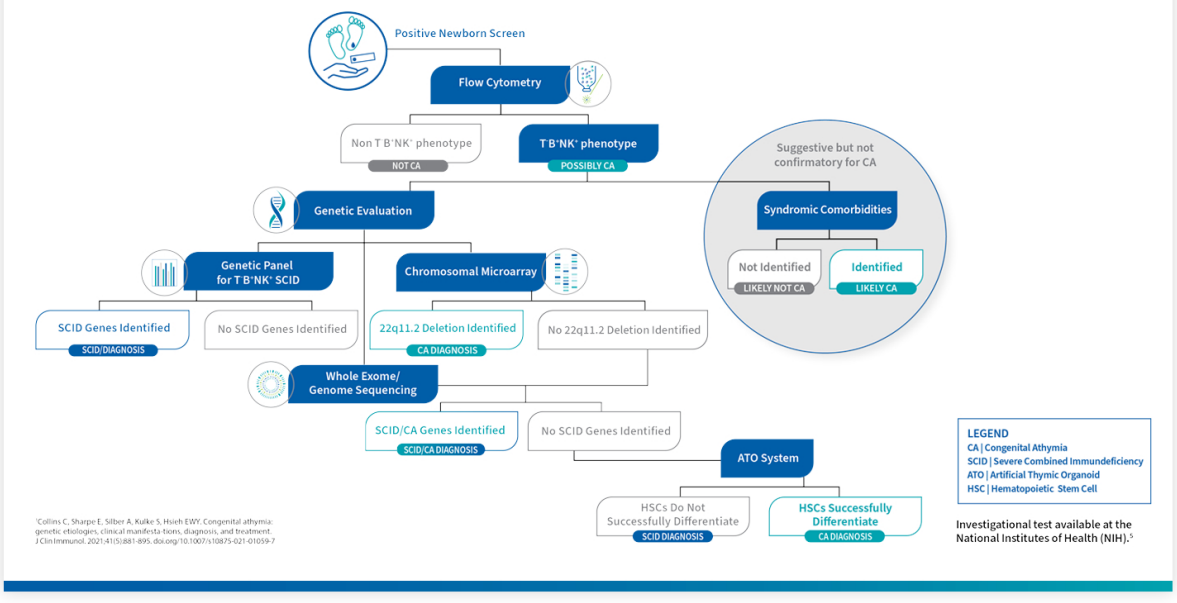
Congenital athymia is initially detected through T-cell receptor rearrangement excision cell circle (TREC) screening[1]. This test will identify infants who may have congenital athymia in addition to severe combined immunodeficiency (SCID) and is required in all 50 U.S. states for all newborns since 2018[1]. TREC screening is critical as it provides the first indication of an immunologic issue in an infant's T-cell development. Low TREC levels indicate the need for further testing[6]. Flow cytometry may show low levels of naive T-cells and may help strengthen the diagnosis of congenital athymia[1].

Congenital athymia and SCID are both primary immunodeficiencies, but they are different[1]. Congenital athymia may be mistaken for SCID, as very low T-cell counts are present in both conditions.

Patients with congenital athymia lack T-cells but have normal numbers of B-cells and natural killer (NK) cells. They present with a T-B+NK+ phenotype. However, a complicating factor is that a subset of patients with SCID also present with a T-B+NK+ phenotype. Additional steps to confirm the diagnosis may be required if a genetic cause of athymia is not identified[1]. SCID is a group of disorders rooted in the dysfunction of hematopoietic stem cells of the bone marrow, not in dysfunction or absence of the thymus. Additionally, patients with SCID may lack B-cells or have impaired B-cell development[1]. In contrast, B-cell numbers are normal in patients with congenital athymia. Lack of B-cells is an important clue that the patient may have SCID. Below is a schematic of the diagnostic pathway including steps for how to differentiate athymia from SCID.

The sooner congenital athymia is identified, the sooner isolation and infection prevention measures can be initiated and the less likely a patient is to be treated with therapies that may not be effective in congenital athymia.

Diagnosing congenital athymia vs. SCID[1]



What is the difference between typical and atypical phenotypes in congenital athymia?

There are 2 phenotypes of congenital athymia: typical and atypical[8]. The typical phenotype is characterized by profound T-cell lymphopenia, absence of rash or lymphadenopathy, and lack of mitogen-stimulated T-cell proliferation[3,8]. The atypical phenotype frequently presents with signs and symptoms of autologous GVHD, such as rash, lymphadenopathy, high numbers of circulating T-cells (from oligoclonal T-cell expansion) and T-cell proliferation in response to mitogens (e.g., phytohemagglutinin)[1].

Often, the expanded oligoclonal T-cells infiltrate the skin, gut, and other organs[8]. Biopsy of the inflammatory rash in patients with atypical congenital athymia shows T-cell infiltrates[1]. Some patients with typical congenital athymia will, over time, develop the atypical phenotype[8].

Understanding Congenital Athymia

As you discuss the care of your patient with their family or caregiver, you may find this additional reading material helpful.

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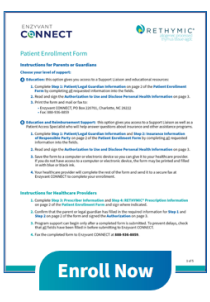

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About RETHYMIC® (allogeneic processed thymus tissue–agdc)

What is RETHYMIC?

RETHYMIC is a regenerative tissue-based therapy that 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).

RETHYMIC is engineered human thymus tissue that is implanted in the thigh muscle to help a child with congenital athymia build a functioning immune system to reduce the number of potentially life-threatening infections. In clinical trials, RETHYMIC demonstrated a survival benefit in some children with congenital athymia. RETHYMIC is a regenerative tissue therapy that was developed to address the ultra-rare condition of congenital athymia, for which, previously, there were no existing treatment options. RETHYMIC has a Regenerative Medicine Advanced Therapy (RMAT) designation from the FDA and it is the first and only FDA-approved regenerative therapy for pediatric congenital athymia.

How does RETHYMIC Work?

RETHYMIC is intended to reconstitute immune system function in patients with congenital athymia. The stem cells in the bone marrow migrate to RETHYMIC. Over time, these stem cells in RETHYMIC begin to develop into infection-fighting T cells. Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6 to 12 months after treatment with RETHYMIC. Once developed, they leave the RETHYMIC processed tissue and enter the bloodstream where they have the ability to interact with other cells.

How Is RETHYMIC Made?

When an infant has cardiac surgery, the surgeon needs to remove some thymus tissue to access the heart. With consent of the infant donor's parents or guardians, the thymus tissue from pediatric cardiac surgeries is donated for the engineering process to make RETHYMIC for use in patients diagnosed with congenital athymia. The manufacturing is a precisely timed 12- to 21-day engineering process in a facility dedicated to making RETHYMIC.

How is RETHYMIC Administered?

RETHYMIC is surgically implanted in the thigh muscle of a child with pediatric congenital athymia. Children are put under general anesthesia and the procedure is performed in an in-patient setting. A surgeon implants the tissue in the child's thigh muscle-a rich source of blood that enables the tissue to get the oxygen and nutrients it needs. RETHYMIC is implanted in one or both thigh muscles. The skin incision is typically approximately 5 cm (2 in) in length.

Clinical Trials

The safety and efficacy of RETHYMIC was evaluated in 105 patients across 10 clinical trials.

LEARN MORE

After Treatment

What to expect after treatment.

LEARN MORE

How to Access

RETHYMIC is currently available at one location in Durham, North Carolina. Here you will find information on accessing RETHYMIC

LEARN MORE

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Clinical Trials

The safety and efficacy of RETHYMIC® (allogeneic processed thymus tissue–agdc) was evaluated in 105 patients across 10 clinical trials. The effectiveness of RETHYMIC was evaluated in 95 of those patients with congenital athymia in 10 clinical trials with follow-up of up to 25.5 years.

The primary end point of the analysis was the Kaplan Meier estimated survival at one year post administration of RETHYMIC. Kaplan Meier estimated survival at two years post treatment was a supportive endpoint. Secondary endpoints included naïve and total T-cell numbers and function at one year post treatment. Reductions in the number of infections over time and survival in patients alive one year post treatment were also analyzed.

Natural History Population

Without treatment, congenital athymia is fatal in childhood. A natural history population was observed from 1991 through 2017 in which 49 patients diagnosed with congenital athymia received supportive care only[5]. The 2-year survival rate was 6%, with all patients dying by 3 years of age.

RETHYMIC Efficacy | Safety | Dosage and Administration

RETHYMIC Efficacy

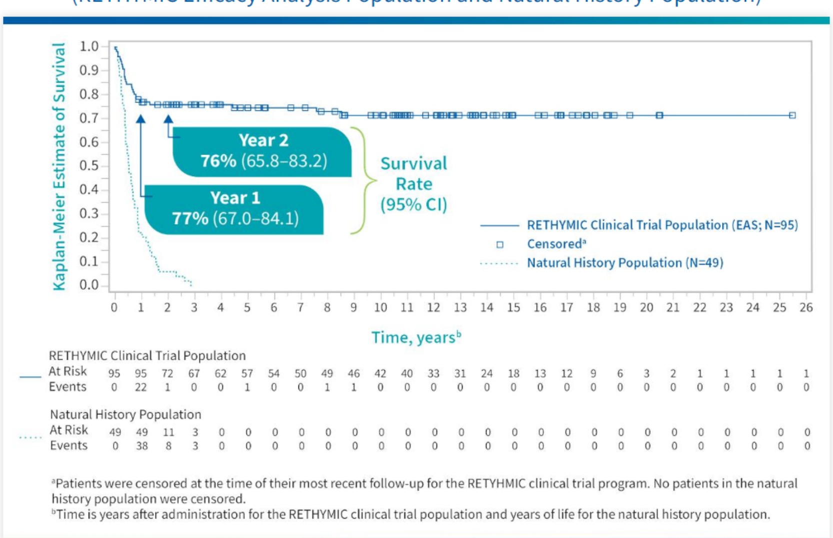
Patient Demographics

Characteristic		Primary Efficacy Analysis (N = 95)
Median (range) age at time of treatment, mo		9 (1-36)
Male, %		59
Race, %	White	70
	Black	22
	Asian/Pacific Islander	4
	American Indian/Alaskan Native	2
	Multi-race	2

RETHYMIC Efficacy

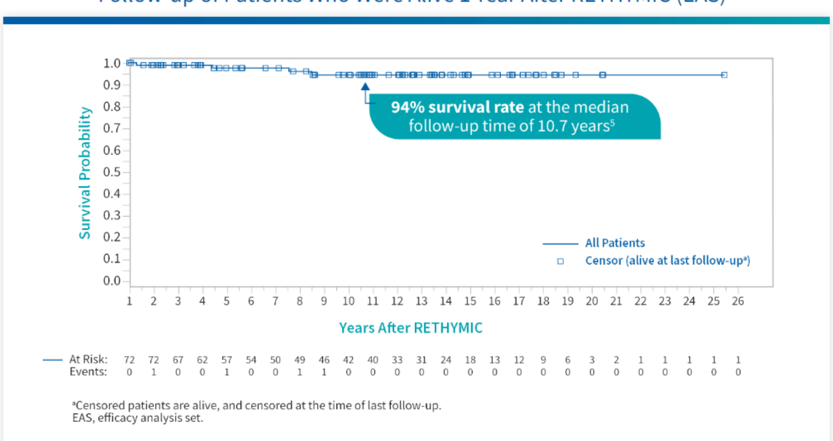
The Kaplan-Meier estimated survival rates at year 1 and year 2 were 77% (95% CI, 0.670-0.841) and 76% (95% CI, 0.658-0.832), respectively[5].

Kaplan-Meier Survival by Year
(RETHYMIC Efficacy Analysis Population and Natural History Population)



For patients who were alive at 1 year after treatment with RETHYMIC, the survival rate was 94% at a median follow-up of 10.7 years[5].

Kaplan-Meier Estimated Survival Rate:
Follow-up of Patients Who Were Alive 1 Year After RETHYMIC (EAS)[3]



Immune System Development

Naive CD4 and CD8T cells reconstituted over the first year following treatment and increased through year 2. Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with RETHYMIC[5].

Development of Naive T-cells Following Treatment
With RETHYMIC in the Primary Efficacy Analysis Population

	Baseline	Month 6	Month 12	Month 24
Median naive CD4+ T cells/mm3 (minimum, maximum) Number of subjects[a]	1.0 (0, 38) 65	42 (0, 653) 67	212 (1, 751) 45	275 (33, 858) 26
Median naive CD8+ T cells/mm3 (minimum, maximum) Number of subjects[a]	0 (0, 46) 59	9 (0, 163) 56	58 (0, 304) 40	86 (6, 275) 26

[a] Enzyvant, Data on File.

2.9

In the first year after treatment with RETHYMIC, the number of patients with an infection event onset 6 to ≤12 months after treatment **decreased by 38%** (from 63 to 39) relative to the number of patients with an infection event onset in the first 6 months post-treatment. A 2-year analysis showed a decrease in both the number of patients with an infection event and the mean number of infection events per patient, with an onset in the first 12 months post-treatment as compared to12 to ≤24 months after treatment. There was a **mean difference of 2.9 events (P<0.001) per patient[5].**

Safety

Adverse Reactions

The safety data described in this section are derived from 10 prospective, single-center, open-label studies, and include 105 patients who were treated with RETHYMIC. The following table lists the adverse reactions occurring in 105 patients who were treated with RETHYMIC in these studies[5].

Adverse Reactions Occuring in at least 5% of Patients
Treated with RETHYMIC During Clinical Studies

System Organ Class Preferred Term	RETHYMIC (N=105) n (%)
Number of Patients with Adverse Reactions[1]	80 (76)
Hypertension (high blood pressure) N=Population	20 (19)
Cytokine release syndrome[2]	19 (18)
Hypomagnesemia (low magnesium)	17 (16)
Rash[3]	16 (15)
Renal impairment / failure[4] (decrease of kidney function)	13 (12)
Thrombocytopenia[5] (low platelets)	13 (12)
Graft versus host disease[6]	11 (10)
Hemolytic anemia[7] (low red bloods cells)	9 (9)
Neutropenia (low white blood cells)	9 (9)
Respiratory distress[8] (difficulty breathing)	8 (8)
Proteinuria (protein in urine)	7 (7)
Pyrexia (fever)	6 (6)
Acidosis[9]	6 (6)
Diarrhea[10]	5 (5)
Seizure[11]	5 (5)

1. Reactions which occurred in the 2 years after treatment.
2. All events (19/19) of cytokine release syndrome occurred in association with ATG-R treatment.
3. Rash includes rash, granuloma skin, rash popular, urticaria.
4. Renal impairment / failure includes renal failure and acute kidney injury, proteinuria and blood creatinine increased.
5. Thrombocytopenia includes thrombocytopenia and Immune thrombocytopenic purpura.
6. GVHD includes GVHD, GVHD-gut, GVHD-skin, Omenn syndrome.
7. Hemolytic anemia includes autoimmune hemolytic anemia, Coombs-positive hemolytic anemia, hemolysis, hemolytic anemia.
8. Respiratory distress includes respiratory distress, hypoxia, respiratory failure.
9. Acidosis includes acidosis, renal tubular acidosis and blood bicarbonate decreased.
10. Diarrhea includes diarrhea and hemorrhagic diarrhea.
11. Seizures include infantile spasms, seizures and febrile convulsion.

The most common (>10%) adverse events related to RETHYMIC included:

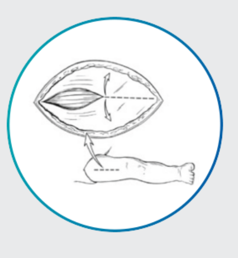
- Hypertension (high blood pressure, 19%)
- Rash (15%)
- Renal impairment / failure (decrease of kidney function, 12%)
- Graft versus host disease (10%)
- Cytokine release syndrome (18%)
- Hypomagnesemia (low magnesium, 16%)
- Thrombocytopenia (low platelets, 12%)

Please see the **Important Safety Information** for RETHYMIC below.

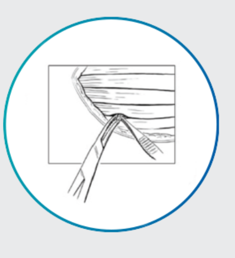
Dosage and Administration

The recommended dose range is 5,000 to 22,000 mm2 of RETHYMIC/m2 recipient body surface area (BSA). RETHYMIC is surgically implanted in one (or both, if necessary) of the patient's quadriceps muscles during a single surgical procedure. The quadriceps muscle is used as the implantation site due to its high vascularization[5].

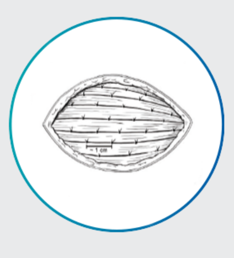
RETHYMIC administration and development of patients T cells[5].



Surgical incision is made over the anterior thigh



RETHYMIC is implanted between muscle fibers



RETHYMIC is covered with muscle tissue

01 After general anesthesia, a ~5 cm long vertical skin incision is made over the anterior thigh compartment

02 Individual slices of RETHYMIC are implanted into pockets between muscle fibers*

03 Each implanted RETHYMIC slice is fully covered by muscle tissue and the pockets stitched closed with a single absorbable suture

04 Following implantation, confirm hemostasis. Close the skin incision with absorbable sutures and apply a standard dressing. Leave the fascia open to allow room for muscle compartment swelling

05 Subsequently, the patient's own bone marrow stem cells migrate to the implanted RETHYMIC, where they develop into naive, immunocompetent T cells

Following administration, capillaries grow from the muscle into RETHYMIC, providing oxygen and nutrients migrating to RETHYMIC, the bone marrow stem cells develop into naive, immunocompetent T-cells[3].

For patients who respond to RETHYMIC, a diverse T-cell population is established. Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6 to 12 months after treatment with RETHYMIC5. For some patients elevated naïve T-cell numbers are not observed until 2 years after treatment. Supportive care measures should be continued until immune reconstitution is established.

HCP RETHYMIC Brochure

Not an actual patient.

Indication and Important Safety Information

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After Treatment

Patients will need to be monitored while their immune system begins to reconstitute. Here are monitoring recommendations and see the RETHYMIC® (allogeneic processed thymus tissue-agdc) **prescribing information** for further information.

How long does it take for RETHYMIC to work?

Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6-12 months after treatment with RETHYMIC[5]. For some patients elevated naïve T-cell numbers are not observed until 2 years after treatment. Supportive care measures should be continued until immune reconstitution is established.

What monitoring needs to be in place?

Monitoring should be performed regularly during the period the immune system is restored. T-cell counts should be checked by flow cytometry every 3 months and, as numbers rise, used to guide weaning of[5]:

- Immunosuppression
- Prophylaxis for pneumocystis
- Reverse isolation

For additional information on monitoring, **please see prescribing information.**

When can the patient receive vaccines?

Immunizations should not be administered in patients who have received RETHYMIC until immune-function criteria have been met. Inactivated vaccines may be administered once all of the following criteria are met[5]:

- Immunosuppressive therapies have been discontinued
- Immunoglobulin (IgG) replacement therapy has been discontinued
- The total CD4+ T-cell count is > 200 cells/mm3 and there are more CD4+ T-cells than CD8+ T cells (CD4+ > CD8+)
- It is recommended that no more than 2 inactivated vaccines be given per month.

Live virus vaccines should not be administered until patients have met the criteria for inactivated vaccines and received vaccinations with inactivated agents (e.g. tetanus toxoid). No additional vaccines (live or inactivated), except the inactivated influenza vaccine, should be given within 6 months after vaccination with a measles-containing vaccine or within 2 months after the varicella vaccine.

Consider verifying response to vaccination with appropriate testing, in particular varicella and measles[5].

When can my patient discontinue immunosuppresants?

Patients can be weaned off immunosuppression when at least 10% of CD3+ T-cells are naïve in phenotype[3].

When can my patient discontinue IgG replacement therapy?

Patients should be maintained on immunoglobulin replacement therapy until all of the following criteria are met:

- No longer on immunosuppression (at least 10% of CD3+ T cells are naïve in phenotype).
- At least 9 months post-treatment.
- Phytohemagglutinin (PHA) response within normal limits
- Normal serum IgA is also desirable but not required.
- Two months after stopping immunoglobulin replacement therapy, the IgG trough level should be checked.
- If the IgG trough level is in the normal range for age, the patient can remain off of immunoglobulin replacement.
- If the IgG trough level is lower than the normal range for age, immunoglobulin replacement therapy should be restarted and continued for a year before being retested using the above guidelines

When can my patient discontinue prophylaxis for pneumocystis?

Prior to and after treatment with RETHYMIC, patients should be maintained on Pneumocystis jiroveci pneumonia prophylaxis until all of the following criteria are met[5]:

- No longer on immunosuppression (at least 10% of CD3+ T cells are naïve in phenotype).
- At least 9 months post-treatment.
- PHA response within normal limits.
- CD4+ T-cell count > 200 cells/mm^3.

How long should isolation continue?

As immunity builds and reaches thresholds for fighting off infection, you may guide families in ending strict isolation. Less restrictive isolation may continue as T-cell levels continue to rise and additional milestones are reached. Restrictive isolation may continue as T-cell levels continue to rise and additional milestones are reached[5,7].

ENZYVANT CONNECT

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ENROLL YOUR PATIENT | VISIT ENZYVANTCONNECT.COM

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How To
Access Treatment

RETHYMIC® (allogeneic processed thymus tissue–agdc) is currently available at one location in Durham, North Carolina.

To obtain the contact information for the single site of administration in Durham, North Carolina, please contact Enzyvant Medical Information at +1 833 369 9868 (833-ENZYVNT) or **medinfo@enzyvant.com**. You can enroll your patient in Enzyvant CONNECT, a program that provides support to patients and families through the treatment journey. **Click here for more information**.

Where is RETHYMIC available?
RETHYMIC is currently available at one location in Durham, North Carolina. Your patient will need to travel to North Carolina for the administration procedure.

How do I access RETHYMIC for my patient?
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When will my patient be treated?
Enzyvant does not make treatment decisions. Enzyvant's role is to supply RETHYMIC. For more information, contact Enzyvant Medical Information at +1 833 369 9868 (833-ENZYVNT) or **medinfo@enzyvant.com**.

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Patient Support

ENZYVANT CONNECT

Supporting the treatment journey

Enzyvant CONNECT is here to provide personalized support throughout your child's treatment journey with RETHYMIC® (allogeneic processed thymus tissue–agdc).

The Enzyvant CONNECT team will assist patients and caregivers with:

- Provide tools to guide caregivers through each step in the treatment journey
- Work with your patients insurer to help caregivers understand insurance coverage for congenital athymia treatment *(Subject to eligibility requirements)*
- Help caregivers understand what, if any, out-of-pocket costs may be expected

Enroll your patient today!

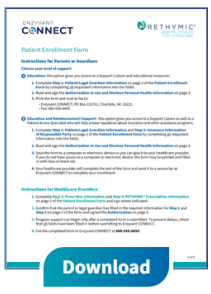
Call us today at 844-ENZCNCT (844-369-2628), 8:00 AM to 8:00 PM ET. Complete and submit the **Patient Enrollment Form** to get started. The form will require your signature, and the signature of a parent or legal guardian of your patient

Access and Support for Families

After you complete and submit your patient's enrollment form, a Patient Access Specialist from Enzyvant CONNECT will contact your patient's family and will schedule a welcome call to review next steps and answer questions.

VISIT ENZYVANTCONNECT.COM

Patient Enrollment Form



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Educational Resources


Jordan, Patient with Congenital Athymia

As you discuss the care of your patient with their family or caregiver, you may find these materials and organizations helpful.

Medical Literature

These articles are provided by Enzyvant for your education and for discussion of FDA-approved use. RETHYMIC® (allogenic processed thymus tissue-agdc) should only be used according to the accompanying complete prescribing information.

LANDMARK STUDY

Experience with cultured thymus tissue in 105 children

Journal of Allergy and Immunology

See Rethymic Full Prescribing Information

Read More

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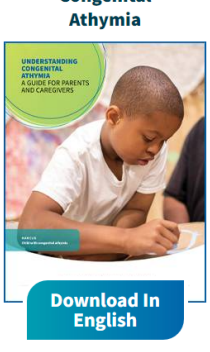

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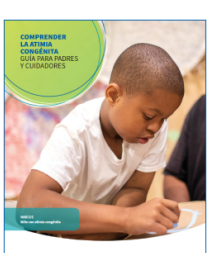

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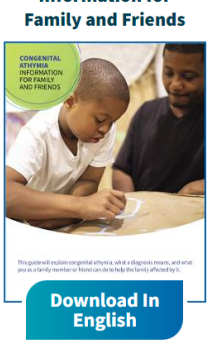
Congenital Athymia: Information for Family and Friends



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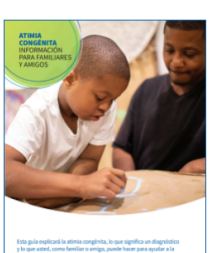

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Caring for a Child with Congenital Athymia

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Congenital Athymia Questions to Ask your Doctor

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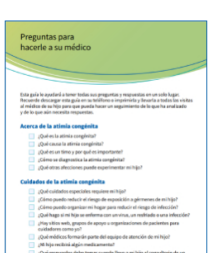

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Patient Organizations

Although no organizations are dedicated specifically to congenital athymia, there are several for patients with immune system diseases that provide valuable support and education. These organizations, independent from Enzyvant, include the following:

Jeffrey Modell Foundation

JEFFREY MODELL FOUNDATION

This nonprofit organization helps families and caregivers affected by immunodeficiency disorders find support, education, awareness, advocacy and care.

VISIT SITE

Global Genes® RARE Foundation Alliance

GLOBAL GENES

Globla Genes is dedicated to eliminating the burdens and challenges of rare diseases for patients and families. A globally connected community equipped to eliminate the challenges of rare disease, united by a determination to support and provide what they need to take action and thrive

VISIT SITE

Immune Deficiency Foundation

IMMUNE DEFICIENCY FOUNDATION

Whether you've been recently diagnosed, have been living with a PI for years, or just think you might have a PI, the Immune Deficiency Foundation (IDF) is here to help. With our support, achieve an early and accurate diagnosis, appropriate treatment, and improved quality of life. IDF programs are meant to connect, engage, and empower families to live longer, stronger, healthier lives.

VISIT SITE

NORD® National Organization for Rare Disorders

NATIONAL ORGANIZATION OF RARE DISORDERS

NORD (National Organization for Rare Disorders), a 501(c)(3) organization, is a patient advocacy organization dedicated to individuals with rare diseases and the organizations that serce them. NORD, along with its more then 300 patient organization members, is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

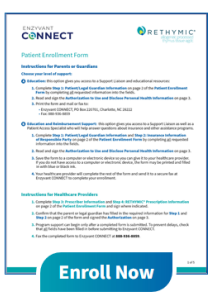
VISIT SITE

ENZYVANT CONNECT

Supporting the Treatment Journey

Enzyvant CONNECT is here to provide education, resources and support throughout your patient's treatment journey.

VISIT ENZYVANTCONNECT.COM



Enroll Now

Indication and Important Safety Information

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. 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

INDICATION

RETHYMIC® (allogeneic processed thymus tissue–agdc) is indicated for immune reconstitution in pediatric patients with congenital athymia. RETHYMIC is not indicated for the treatment of patients with severe combined immunodeficiency (SCID).

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