

## A caregiver's guide to **RETHYMIC**.



**JADA**

Patient with  
congenital athymia



### **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 on pages 9 & 10, and click here for [RETHYMIC Product Information](#).

Lean on your family and friends and advocate for your child as best as you can.

AMANDA M.  
JADA'S MOTHER



## What is congenital athymia?

Congenital athymia is an ultra-rare immune condition in which a child is born without a thymus.<sup>1</sup> The thymus is an organ that sits on top of the heart and plays a critical role in helping the immune system work.<sup>1</sup> The immune system is made of organs, cells, and proteins that work together throughout the body to fight infections.<sup>2</sup> One important cell is the T cell, which is a type of white blood cell that attacks and remembers foreign invaders such as viruses, bacteria, fungi, and parasites.<sup>3</sup> The T in T cell stands for thymus.<sup>3</sup> T cells begin in the bone marrow as T-cell precursors. Then they travel to the thymus where they are selected for their ability to distinguish foreign invaders. The naive T cells are released into the bloodstream as part of an infection-fighting army.<sup>1</sup>

Children with congenital athymia can face repeated infections because they do not have enough working T cells to fight the invaders off.<sup>1</sup> These infections can be fatal.<sup>1</sup> Without working T cells, children can also be affected by autoimmune conditions, when the body's immune system attacks and destroys healthy body tissue by mistake.<sup>4</sup> With only supportive care, children with congenital athymia typically do not survive beyond 2 to 3 years of age.<sup>5</sup>

### 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.

**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.

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## What is RETHYMIC?

RETHYMIC is engineered human thymus tissue that is implanted into the thigh muscle to help a child with congenital athymia build a functioning immune system to reduce the risk of potentially life-threatening infections.<sup>6</sup> 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.<sup>7</sup>

## How is RETHYMIC made?

The thymus is an organ that sits on top of the heart.<sup>1</sup> 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.<sup>8</sup>

The manufacturing is a precisely timed 12- to 21-day engineering process in a facility dedicated to making RETHYMIC.<sup>8</sup>



**BRYNLEE**  
**PATIENT 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.

**Cytomegalovirus (CMV) Infection:** In clinical studies with RETHYMIC, 3 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.

**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.

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## How does my child receive RETHYMIC?

RETHYMIC is surgically implanted in the recipient's thigh muscle. The thigh muscle is used because its good blood supply provides oxygen and nutrients to RETHYMIC.<sup>9</sup>

**The procedure to administer RETHYMIC takes approximately 2 hours while the patient is under general anesthesia.<sup>6</sup>**

## How does RETHYMIC work?

RETHYMIC is intended to reconstitute immune function in patients with congenital athymia.<sup>6</sup> 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.<sup>6</sup> Once developed, they leave RETHYMIC and enter the bloodstream, where they have the ability to interact with other cells.<sup>2</sup>

**RETHYMIC is available at one location in Durham, North Carolina.**

**Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6 to 12 months after treatment with RETHYMIC. For some patients it may take up to 2 years after treatment to see higher numbers of T cells.**



### **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.

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## What happens after treatment?

After treatment with RETHYMIC, your child will need to be monitored carefully to ensure that he or she avoids infection and other complications.<sup>9</sup> After your child is discharged from the surgical unit, he or she should return to the care of their local healthcare team.<sup>8</sup>

Immune reconstitution sufficient to protect from infection is unlikely to develop prior to 6 to 12 months after treatment with RETHYMIC. For some patients it may take up to 2 years after treatment to see higher numbers of T cells.<sup>6</sup>

Your child's doctor will check T-cell counts regularly to gauge the success of treatment. During this time, you'll want to continue strict isolation measures to avoid risk of infections.<sup>8</sup>

However, even after your child has demonstrated the ability to fight off infection, he or she will still need to be monitored on a regular basis by an immunologist.<sup>9</sup>

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.



You are encouraged to report suspected side effects to the FDA at 1-800-FDA-1088 or [www.fda.gov/safety/medwatch](http://www.fda.gov/safety/medwatch), or contact Enzyvant at 833-369-9868.

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**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.

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## The effectiveness of RETHYMIC.

The effectiveness of RETHYMIC was evaluated in 95 patients with congenital athymia in 10 clinical trials, with follow-up of up to 25.5 years.<sup>6</sup>

### RETHYMIC clinical trials showed<sup>6</sup>

Estimated survival at year 1  
after treatment was

**77%**

Estimated survival at year 2  
after treatment was

**76%**

**94%**

For patients who were alive at 1 year after treatment, the survival rate was **94% at a median follow-up of 10.7 years<sup>6</sup>**

## Decrease in infections.

RETHYMIC significantly reduced the number of infections over time.<sup>6</sup>

### **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.

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## The safety of RETHYMIC was studied in clinical trials.

The safety of RETHYMIC has been examined in 10 clinical studies of 105 patients.<sup>6</sup>

The most common side effects with RETHYMIC are:

- **Hypertension (high blood pressure)**
- **Cytokine release syndrome (systemic inflammation with fever and multiple organ dysfunction)**
- **Rash**
- **Hypomagnesemia (low magnesium)**
- **Renal impairment/failure (decrease in kidney function)**
- **Thrombocytopenia (low platelets)**
- **Graft versus host disease**

Be sure to tell your child's doctor about any side effect that bothers your child or does not go away after treatment with RETHYMIC.

**These are not all of the possible side effects of RETHYMIC.  
Please see pages 9 & 10 for additional important  
information on the safety of RETHYMIC.**

### **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.

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# ENZYVANT CONNECT

## Supporting the treatment journey

Enzyvant CONNECT is a program for patients and caregivers that provides personalized support throughout their treatment journey.

The Enzyvant CONNECT team will assist families with:

- **Navigating insurance information**
- **Connecting to financial assistance programs**
- **Providing educational resources**

**To find out more, call Enzyvant CONNECT:**

**844-ENZCNCT (844-369-2628)**

**Monday through Friday, 8:00 AM to 8:00 PM ET**

## Patient advocacy and support organizations

Patient advocacy and support organizations are working to support patients and families.

Several organizations provide valuable support and education for patients with immune system diseases. These organizations are listed by name and website.

**Jeffrey Modell Foundation (JMF):**

<https://www.info4pi.org>

**Immune Deficiency Foundation (IDF):**

<https://primaryimmune.org>

**National Organization for Rare Disorders (NORD):**

<https://rarediseases.org>

**Global Genes:**

<https://globalgenes.org>



*Not an actual patient*

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**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](http://www.fda.gov/safety/medwatch).

For more information, please visit [RETHYMIC.com](http://RETHYMIC.com)

#### References:

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