REBLOZYL is a prescription medicine used to treat anemia (low red blood cells) in adults with beta thalassemia who need regular red blood cell (RBC) transfusions.

REBLOZYL is not for use as a substitute for RBC transfusions in people who need immediate treatment for anemia. It is not known if REBLOZYL is safe or effective in children.

Living with beta (β) thalassemia

YOUR GUIDE TO STARTING REBLOZYL

Before receiving REBLOZYL, tell your healthcare provider about all of your medical conditions, including if you:

- have or have had blood clots
- have or have had high blood pressure (hypertension)
- take hormone replacement therapy or birth control pills (oral contraceptives)
- have had your spleen removed (splenectomy)
- smoke

Please see full Prescribing Information and Patient Information, for REBLOZYL.

Reblozyl®
(luspatercept-aamt)
for injection 25mg • 75mg

WELCOME TO REBLOZYL

Your doctor has prescribed REBLOZYL because he or she thinks it's the right treatment for managing anemia* associated with your β-thalassemia. REBLOZYL is different and you might have some questions. This guide is here to help give you some answers about β-thalassemia and your course of treatment with REBLOZYL.

Here's what you'll find inside:

About β-thalassemia

4 About β-thalassemia
5 Types of β-thalassemia
6 Understanding anemia

About REBLOZYL

7 What is REBLOZYL (REB-low-zil)?
8 How was REBLOZYL studied?
9 Characteristics of the 336 patients in the clinical trial
10 What are the possible benefits of REBLOZYL?
11 What are the possible side effects of REBLOZYL?
12 How do I receive REBLOZYL?
13 How long might I receive treatment with REBLOZYL?

Resources

14 Glossary and resources for people with β-thalassemia
15 Celgene Patient Support®

Visit REBLOZYL.com to learn more

*Words in the glossary are **bold** and **blue** at first mention.

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BEFORE RECEIVING REBLOZYL, TELL YOUR HEALTHCARE PROVIDER ABOUT ALL OF YOUR MEDICAL CONDITIONS, INCLUDING IF YOU:

- are pregnant or plan to become pregnant. REBLOZYL may harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with REBLOZYL.

  Females who are able to become pregnant:
  — Your healthcare provider should do a pregnancy test before you start treatment with REBLOZYL.
  — You should use effective birth control (contraception) during treatment with REBLOZYL and for at least 3 months after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if REBLOZYL passes into your breast milk.
  — Do not breastfeed during treatment with REBLOZYL and for 3 months after the last dose. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements

ABOUT β-THALASSEMIA

β-thalassemia is an inherited blood disorder

β-thalassemia (BAY-tah THAL-a-SEE-mee-ah) is an inherited condition, which means it is passed down from parents to children. It is a disorder that can lead to anemia, which is a low number of **red blood cells** or a low amount of **hemoglobin**, the oxygen-carrying molecule in red blood cells. Roughly 55% of patients are older than 20 years (average age 23.2 years).

What causes β-thalassemia?

In people with β-thalassemia, hemoglobin may not be made correctly. Normal, healthy hemoglobin includes 2 sets of 2 different proteins: an alpha and a beta. In many people with β-thalassemia, "**beta globin**" proteins are not formed correctly. If your body does not produce enough of either protein, red blood cells do not form properly and cannot carry the oxygen your organs need to stay healthy. This could result in anemia, which may be severe enough to require **red blood cell transfusions**.

β-thalassemia can cause symptoms of anemia and other conditions

If you have anemia, you may feel tired, weak, or have pale skin. Your doctor will measure hemoglobin to help determine if you have anemia. When you have anemia due to β-thalassemia, there can be complications, such as an enlarged spleen or brittle bones.

- If anemia causes the spleen to become enlarged, some people with β-thalassemia will have it removed through a surgery called a splenectomy

TYPES OF β-THALASSEMIA

Many people with β-thalassemia rely on red blood cell transfusions

Red blood cell transfusions are a primary option for treating anemia in people with β-thalassemia. Transfusions add new, working red blood cells to your body from a donor. They temporarily replace red blood cells and help increase hemoglobin, but do not help your body produce more.

Red blood cells are rich in iron, so repeated transfusions may result in iron collecting abnormally in organs like your heart, liver, spleen, or endocrine glands. This buildup can prevent these organs from working properly, so a treatment called a "**chelating agent**" is often used to remove this excess iron.

Types of β-thalassemia that may require red blood cell transfusions

β-thalassemia intermedia	β-thalassemia major (Cooley's anemia)
People with β-thalassemia intermedia have anemia symptoms that vary in degree, ranging from mild to severe anemia	People with β-thalassemia major begin to show severe anemia symptoms during infancy and need regular red blood cell transfusions and continuous medical care
Many people with β-thalassemia intermedia eventually require regular red blood cell transfusions	Because people with β-thalassemia major cannot make enough working red blood cells, they are dependent on regular red blood cell transfusions

UNDERSTANDING ANEMIA

Anemia occurs in patients with β-thalassemia in 3 ways:

1. Low or absent production of hemoglobin

2. Red blood cells break down faster than normal

3. Fewer mature, working red blood cells

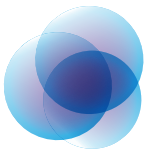
Why some people with β-thalassemia have too few mature, working red blood cells

Mature red blood cells are produced in **bone marrow** through a process called **erythropoiesis**. In people with β-thalassemia, not enough immature red blood cells (**erythroid cells**) are able to mature and leave the bone marrow. These erythroid cells are unable to do the job of fully working, mature red blood cells, which is to carry oxygen throughout the body.

- When erythroid cells start to pile up in the bone marrow, they can prevent mature, working red blood cells from developing

The term for when red blood cells are unable to fully mature or develop before leaving the bone marrow is "**ineffective erythropoiesis**"

- This low production of mature, working red blood cells leads to low levels of hemoglobin and symptoms of anemia



Your doctor has prescribed REBLOZYL because he or she thinks it's the right treatment for managing your anemia

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WHAT IS REBLOZYL (*REB-low-zil*)?

REBLOZYL is a prescription medicine used to treat anemia (low red blood cells) in adults with beta thalassemia who need regular red blood cell (RBC) transfusions.

REBLOZYL is not for use as a substitute for RBC transfusions in people who need immediate treatment for anemia. It is not known if REBLOZYL is safe or effective in children.

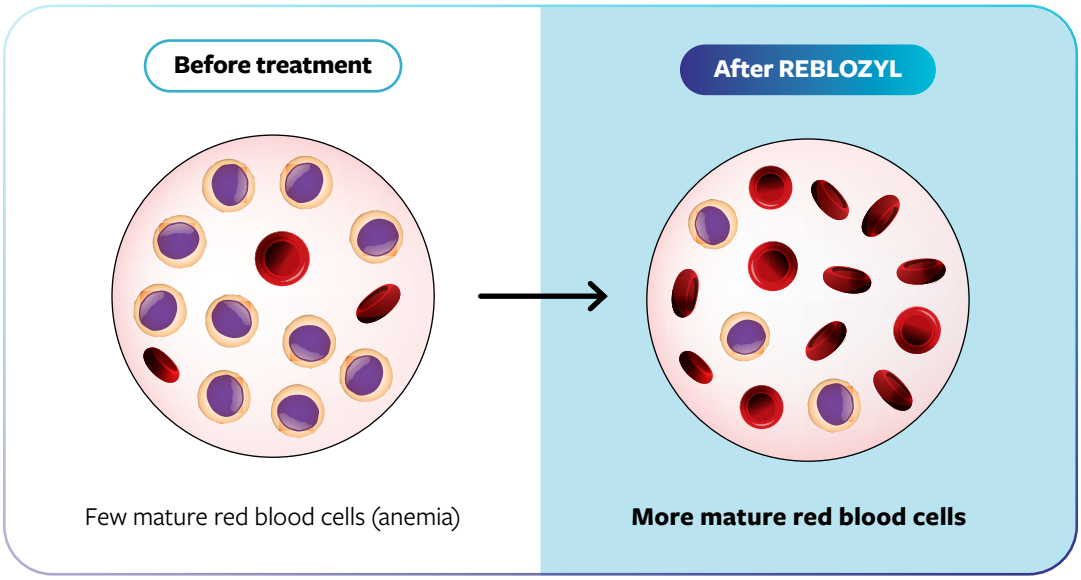
REBLOZYL is the first and only erythroid maturation agent

REBLOZYL is called an **erythroid maturation agent** because it helps erythroid cells develop and become mature, working red blood cells. This may result in a greater number of healthy red blood cells and improve anemia.

HOW DOES REBLOZYL WORK?

REBLOZYL works by developing more mature, working red blood cells

REBLOZYL allows more immature cells to mature and work properly. The amount of hemoglobin increased and the quality of red blood cells improved as patients received treatment with REBLOZYL. This means that there are more mature red blood cells in the bloodstream.



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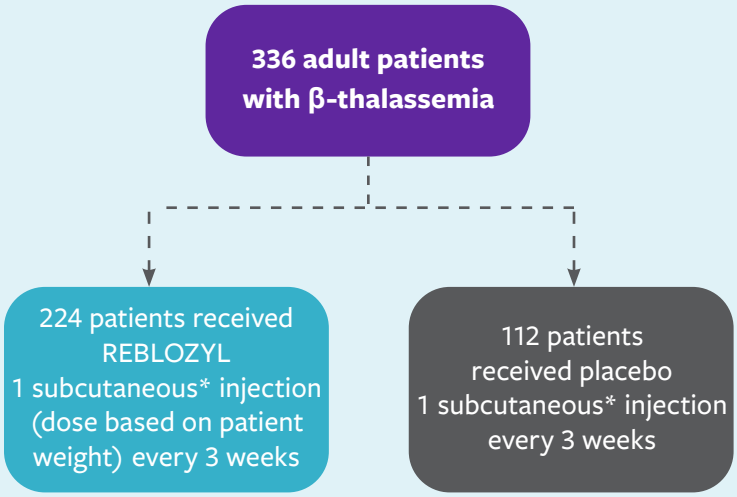
HOW WAS REBLOZYL STUDIED?

The clinical trial compared REBLOZYL to placebo (no active medication)

- This trial included adults with β-thalassemia who needed regular red blood cell transfusions of 6 to 20 units every 24 weeks

The main goal of the study was to see if REBLOZYL could reduce transfusion burden by at least one-third (at least 2 red blood cell units) during a set 12-week period (weeks 13–24)

Patients in the clinical trial were divided into 2 groups:



All patients in both arms were allowed to receive best supportive care as needed, which included:

- Red blood cell transfusions
- Iron-chelating agents
- Antibiotics, antivirals, antifungals
- Nutritional support

* **Subcutaneous** means under the skin.

Patients included in the study needed to:

- Receive regular red blood cell transfusions (6–20 red blood cell units per 24 weeks) with no transfusion-free period greater than 35 days during that period
- Be at least 18 years old

Patients could not be part of the study if they had:

- Hemoglobin S/β-thalassemia or alpha (α)-thalassemia
- Major organ damage (liver disease, heart disease, lung disease, poor kidney function)
- Recent deep vein **thrombosis** or stroke or recent use of **erythropoiesis-stimulating agent**, **immunosuppressant**, or **hydroxyurea** therapy

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CHARACTERISTICS OF THE 336 PATIENTS IN THE CLINICAL TRIAL

Age range:

18 to **66** years

30 years was the **median** age

Median is the middle of a range of numbers

Gender:

58% of patients **(195 out of 336 patients)** were women and **42%** of patients **(141 out of 336 patients)** were men

Mutation type:

31% of patients **(103 out of 336 patients)** had a β0/β0 **mutation**

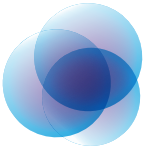
This means that their bodies produced no normal adult hemoglobin

Splenectomy:

58% of patients **(194 out of 336 patients)** had their spleen removed

Transfusion burden at the start of the trial:

Patients received approximately 6 red blood cell units every 12 weeks (median transfusion burden; range 3–14 units every 12 weeks)



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WHAT ARE THE POSSIBLE BENEFITS OF REBLOZYL?

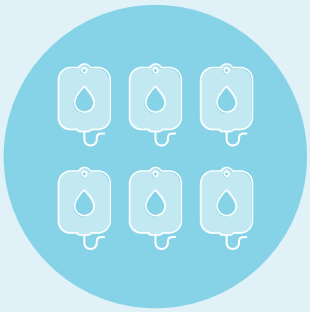
The main goal of the clinical trial

The main goal of the study was to see if REBLOZYL could reduce transfusion burden by at least one-third (at least 2 red blood cell units) during a set 12-week period (weeks 13–24)

- Reducing transfusion burden could mean fewer red blood cell units per transfusion or a reduction in the visits needed for transfusions

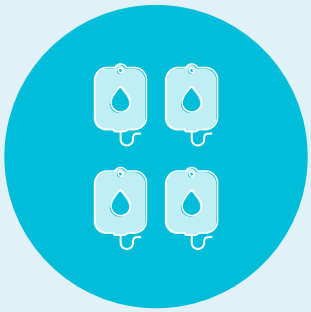
Example patient

For example, if a patient needed 6 red blood cell units every 12 weeks before the trial...



After receiving REBLOZYL

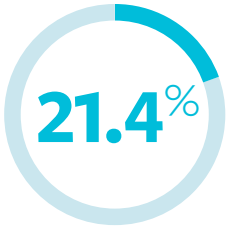
...this patient may only need 4 (or less) red blood cell units during weeks 13 to 24



REBLOZYL helped more patients have fewer red blood cell transfusions

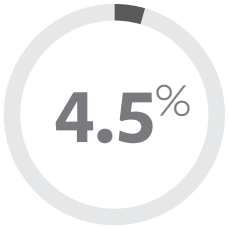
Patients who had their red blood cell transfusion burden reduced by one-third during weeks 13 to 24:

More than 1 in 5 patients on REBLOZYL had their transfusion burden reduced by a third over 12 weeks



of patients receiving REBLOZYL (48 patients out of 224)

vs



of patients receiving placebo (5 patients out of 112)

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WHAT ARE THE POSSIBLE SIDE EFFECTS OF REBLOZYL?

REBLOZYL may cause serious side effects, including:

- **Blood clots.** Blood clots in the arteries, veins, brain, and lungs have happened in people with beta thalassemia during treatment with REBLOZYL. The risk of blood clots may be higher in people who have had their spleen removed or who take hormone replacement therapy or birth control (oral contraceptives). Call your healthcare provider or get medical help right away if you have any of these symptoms:
  - — chest pain
  - — trouble breathing or shortness of breath
  - — pain in your leg, with or without swelling
  - — a cold or pale arm or leg
  - — sudden numbness or weakness that are both short-term or continue to happen over a long period of time, especially on one side of the body
  - — severe headache or confusion
  - — sudden problems with vision, speech, or balance (such as trouble speaking, difficulty walking, or dizziness)
- **High blood pressure.** REBLOZYL may cause an increase in your blood pressure. Your healthcare provider will check your blood pressure before you receive your REBLOZYL dose. Your healthcare provider may prescribe you medicine to treat high blood pressure or increase the dose of medicine you already take to treat high blood pressure, if you develop high blood pressure during treatment with REBLOZYL.

The most common side effects of REBLOZYL include:

- tiredness
- muscle or bone pain
- dizziness
- diarrhea
- stomach (abdominal) pain
- allergic reactions
- headache
- joint pain (arthralgia)
- nausea
- cough
- trouble breathing

REBLOZYL may cause fertility problems in females. This could affect your ability to become pregnant. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of REBLOZYL. Call your doctor for medical advice about side effects. You are encouraged to report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Tell your healthcare team about any side effect(s) you may experience

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HOW DO I RECEIVE REBLOZYL?

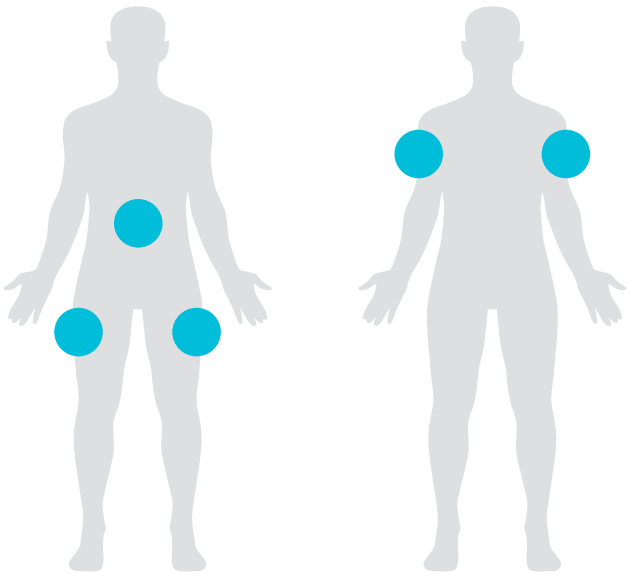
REBLOZYL will be given to you by a healthcare professional

- REBLOZYL is given as an injection under the skin (subcutaneous) with a needle. Needles used for injections under the skin are smaller than those used for injections into muscle (intramuscular)
- Your healthcare provider will prescribe REBLOZYL in a dose that is right for you. Your healthcare provider will calculate the exact dose of REBLOZYL you will need based on your weight, and you will receive it once every 3 weeks in a doctor's office
- Your doctor or another healthcare provider will check your hemoglobin levels each time before you receive REBLOZYL, and may increase or decrease your dosing amount or adjust your dosing schedule based on the results
- **If your scheduled REBLOZYL dose is delayed or missed, your healthcare provider will give your dose of REBLOZYL as soon as possible and continue your treatment as prescribed with at least 3 weeks between doses**

Where will REBLOZYL be injected?

- REBLOZYL is given as an injection under your skin (subcutaneous) by your healthcare provider
  - The injection may be given in the upper arm, thigh, or abdomen

Possible injection sites



Front **Back**

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HOW LONG MIGHT I RECEIVE TREATMENT WITH REBLOZYL?

You should receive REBLOZYL as long as your doctor finds it is working for you and you are able to tolerate any potential side effects that may occur

- Your healthcare provider may adjust your dose or stop treatment depending on how you respond to REBLOZYL
- Your healthcare provider will decide when you should receive REBLOZYL based on your response, which will include your current symptoms and any reduction in your need for red blood cell transfusions, so be sure to follow his or her instructions
- Your healthcare provider may consider a dose increase based on how you respond to REBLOZYL
- Your healthcare provider may also decrease your dose or stop your dose if you experience certain side effects or no reductions in transfusions

What was the dosing experience in the clinical trial?

In the clinical trial, more than half of the patients received REBLOZYL for at least 63.3 weeks

Side effects caused 2.7% of patients to have a reduced dose of REBLOZYL and 15.2% to have a dose of REBLOZYL interrupted

Almost half (46%) of patients who received REBLOZYL had their dose increased

5.4% of patients discontinued REBLOZYL due to side effects

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GLOSSARY

Anemia: Low red blood cell count

Beta globin: A protein building block of hemoglobin

Blood pressure: The force of circulating blood on the walls of blood vessels

Bone marrow: The soft interior of the bones where new blood cells are created

Chelating agent: A chemical compound used to remove toxic metals from the body

Erythroid cell: An immature red blood cell

Erythroid maturation agent: Treatment that helps young cells become mature cells

Erythropoiesis: The formation of red blood cells in blood-forming tissue within the bone marrow

Erythropoiesis-stimulating agent: A manufactured growth hormone that helps the body produce more immature red blood cells

Hemoglobin: Oxygen-carrying protein found in red blood cells

Hydroxyurea: A type of medicine used to treat certain cancers

Immunosuppressant: An agent that decreases the body's immune response

Ineffective erythropoiesis: The inability of oxygen-carrying red blood cells to leave the bone marrow

Ischemic stroke: The most common type of stroke, caused by a blood clot that blocks a blood vessel in the brain

Median: A statistics term. The middle of a range of numbers

Mutation: An abnormal change within a gene

Placebo: An inactive substance that looks the same as, and is given the same way as, an active drug or treatment being tested

Red blood cells (RBCs): Blood cells that carry oxygen from the lungs to all cells in the body

Red blood cell transfusion: A process that adds red blood cells into the bloodstream

Subcutaneous: Under the skin

Thromboembolic event: Formation of a clot in a vein or artery that breaks loose and is carried by the blood to block a blood vessel

Thrombosis: Formation of a blood clot

Uric acid: A chemical created when the body breaks down certain substances made by the body and found in some foods and drinks and is removed from the body by the kidneys. Too much uric acid in your body can cause you to become sick

RESOURCES FOR PEOPLE WITH β-THALASSEMIA

The following organizations* provide disease education, additional support, and expert opinions.

*This list of independent organizations is provided as an additional resource for obtaining information. Inclusion on this list does not indicate endorsement by Bristol-Myers Squibb Company or Acceleron Pharma Inc. of an organization or its communications.

Cooley's Anemia Foundation
(212) 279-8090
https://www.thalassemia.org

Thalassaemia International Federation (TIF)
+357 22 319 129
https://thalassaemia.org.cy/about

The Centers for Disease Control and Prevention
https://www.cdc.gov/ncbddd/thalassemia/index.html

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CELGENE PATIENT SUPPORT®

CELGENE PATIENT SUPPORT®

A single source for access support

Learn about financial help for REBLOZYL

At Celgene Patient Support®, we care about making sure you get the help you need to start your treatment. Our Specialists are here to help you and your loved ones understand the programs and services that may be available to you.

Programs that help with the cost of REBLOZYL differ by the type of insurance you have. Even if you don't have insurance or enough coverage to pay for your medicine, financial help may be available.

Financial assistance

There are programs and organizations that may help pay for REBLOZYL, depending on your insurance situation.

Celgene Commercial Co-pay Program

Co-pay responsibility for REBLOZYL is reduced to $0 (subject to annual benefit limits) for eligible patients with commercial or private insurance (including healthcare exchanges).*

Celgene Patient Assistance Program (PAP)

REBLOZYL may be available at no cost for qualified patients who are uninsured or underinsured.†

If you are unable to afford your medication (including patients with Medicare, Medicaid, or other government-sponsored insurance), you may be able to receive help from independent third-party organizations.‡

Enrolling in Celgene Patient Support®

Visit us at
www.celgenepatientsupport.com

Email us at **patientsupport@celgene.com**
or fax to **1-800-822-2496**

For more information on Celgene Patient Support®

Call us at **1-800-931-8691**,
Monday – Friday, 8 AM – 8 PM ET
(*translation services available*)

*Other eligibility requirements and restrictions apply. Please see full Terms and Conditions on the Celgene Patient Support® website.

†Patients must meet specified financial and insurance eligibility requirements to qualify for assistance. Please see Eligibility Requirements on the Celgene Patient Support® website.

‡Financial and medical eligibility requirements vary by organization.

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For more information on REBLOZYL and to access helpful resources, visit

www.REBLOZYL.com

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