

A large, teal-colored stylized letter 'C' is positioned on the left side of the page. It has a red and white striped segment at the top right and a red and black striped segment at the bottom left. The text "A GUIDE TO YOUR TREATMENT JOURNEY" is centered within the 'C' in a bold, dark blue, uppercase sans-serif font.

A GUIDE TO YOUR TREATMENT JOURNEY

Please see Important Safety Information on page 5 and full Prescribing Information, including Patient Information, for CASGEVY.

STARTING THE CASGEVY™ JOURNEY

CASGEVY is a one-time* **gene therapy** for people aged 12 years and older living with beta thalassemia (β -thalassemia) who need regular blood transfusions. This is called transfusion-dependent beta thalassemia (or TDT). Before you begin your CASGEVY journey, it's important to understand the treatment process and talk with your healthcare team about what to expect along the way. This guide will walk you through each step and give you a picture of the road ahead.

As you consider CASGEVY, you'll want to meet with your support network and healthcare team to discuss treatment and all that's involved. This will give you time to ask questions and make sure you have the right support in place.

Everyone's experience is different, and treatment timing will vary. The entire process could take up to a year.

To help you along your journey, hold onto this guide and refer back to it as you go through treatment.



Glossary of words to know

Certain words used in this guide or by your healthcare team may be new to you. These terms are **bold and underlined in red** throughout this brochure. You can find definitions of those key treatment terms in the Glossary section.

INDICATION AND IMPORTANT SAFETY INFORMATION

What is CASGEVY?

CASGEVY is a one-time therapy used to treat people aged 12 years and older with beta thalassemia (β -thalassemia) who need regular blood transfusions.

CASGEVY is made specifically for each patient, using the patient's own edited blood stem cells, and increases the production of a special type of hemoglobin called hemoglobin F (fetal hemoglobin or HbF). Having more HbF increases overall hemoglobin levels and has been shown to improve the production and function of red blood cells. This can eliminate the need for regular blood transfusions in people with beta thalassemia.

What is the most important information I should know about CASGEVY?

After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections). Your doctor will monitor this and give you treatment as required. The doctor will tell you when blood cell levels return to safe levels.

*Treatment involves a multi-step process. This includes the collection and editing of blood stem cells to make your CASGEVY. It also includes preparing you for CASGEVY, administration of CASGEVY, and follow-up monitoring for potential side effects, and recovery.



YOUR AUTHORIZED TREATMENT CENTER

Everyone who receives CASGEVY[™] will receive treatment at an Authorized Treatment Center,* or ATC.

Your ATC is where you will go for appointments and to meet with your healthcare team. Your healthcare provider at the ATC will help you decide if CASGEVY is right for you. A locator tool is available at [CASGEVY.com](https://www.casgevyy.com) to help you find an ATC near you.

ATC Name:

Address:

Phone:

*ATCs are independently owned and operated. Vertex does not have any oversight of any ATC, and Vertex does not endorse or recommend any particular ATC. The decision for determining which ATC to select for treatment lies with you and your healthcare provider.



YOUR HEALTHCARE TEAM

Use this page to fill out the contact information for the members of your healthcare team. You can refer back to this when contacting your healthcare providers.

Name / Role:

Contact:

Name / Role:

Contact:

Name / Role:

Contact:

Name / Role:

Contact:

Name / Role:

Contact:

Name / Role:

Contact:

INDICATION AND IMPORTANT SAFETY INFORMATION

What is CASGEVY™?

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What is the most important information I should know about CASGEVY?

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- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of platelet cells:
 - severe headache
 - abnormal bruising
 - prolonged bleeding
 - bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood
- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of white blood cells:
 - fever
 - chills
 - infections

You may experience side effects associated with other medicines administered as part of the treatment regimen with CASGEVY. Talk to your physician regarding those possible side effects. Your healthcare provider may give you other medicines to treat your side effects.

How will I receive CASGEVY?

Your healthcare provider will give you other medicines, including a conditioning medicine, as part of your treatment with CASGEVY. It's important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

After receiving the conditioning medicine, it may not be possible for you to become pregnant or father a child. You should discuss options for fertility preservation with your healthcare provider before treatment.

STEP 1: Before CASGEVY treatment, a doctor will give you mobilization medicine(s). This medicine moves blood stem cells from your bone marrow into the blood stream. The blood stem cells are then collected in a machine that separates the different blood cells (this is called apheresis). This entire process may happen more than once. Each time, it can take up to one week.

During this step, rescue cells are also collected and stored at the hospital. These are your existing blood stem cells and are kept untreated just in case there is a problem in the treatment process. If CASGEVY cannot be given after the conditioning medicine, or if the modified blood stem cells do not take hold (engraft) in the body, these rescue cells will be given back to you. If you are given rescue cells, you will not have any treatment benefit from CASGEVY.

STEP 2: After they are collected, your blood stem cells will be sent to the manufacturing site where they are used to make CASGEVY. It may take up to 6 months from the time your cells are collected to manufacture and test CASGEVY before it is sent back to your healthcare provider.

STEP 3: Shortly before your stem cell transplant, your healthcare provider will give you a conditioning medicine for a few days in hospital. This will prepare you for treatment by clearing cells from the bone marrow, so they can be replaced with the modified cells in CASGEVY. After you are given this medicine, your blood cell levels will fall to very low levels. You will stay in the hospital for this step and remain in the hospital until after the infusion with CASGEVY.

STEP 4: One or more vials of CASGEVY will be given into a vein (intravenous infusion) over a short period of time.

After the CASGEVY infusion, you will stay in hospital so that your healthcare provider can closely monitor your recovery. This can take 4-6 weeks, but times can vary. Your healthcare provider will decide when you can go home.

What should I avoid after receiving CASGEVY?

- Do not donate blood, organs, tissues, or cells at any time in the future

What are the possible or reasonably likely side effects of CASGEVY?

The most common side effects of CASGEVY include:

- Low levels of platelet cells, which may reduce the ability of blood to clot and may cause bleeding
- Low levels of white blood cells, which may make you more susceptible to infection

Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells). Tell your healthcare provider right away if you get any of the following symptoms:

- fever
- chills
- infections
- severe headache
- abnormal bruising
- prolonged bleeding
- bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CASGEVY

Talk to your healthcare provider about any health concerns.

TREATMENT OVERVIEW

- The entire CASGEVY[™] treatment journey could take up to a year
- Location of the steps in this brochure is based on the clinical study
- Your healthcare team will help map out a treatment plan that works for you and your support network, including making sure the key dates in the timeline work with your schedules
- Your red blood cell transfusions will continue throughout the treatment journey until you have received CASGEVY as determined by your healthcare provider



The following pages include more details about each of the 6 steps. You can continue to refer to each of the steps as you get further along in your own treatment journey.

*Step 3 may need to be repeated as multiple cell collections are sometimes needed.



STEP 1 DECIDING ON CASGEVY[™]

The first step in your journey is to talk with a healthcare provider about CASGEVY. If you and your healthcare team feel CASGEVY might be an option for you, you will need to schedule an appointment at an Authorized Treatment Center (ATC). CASGEVY is only available at ATCs.



WHAT TO EXPECT

You may need to travel to your nearest ATC and potentially find a place nearby to stay.

If you and your healthcare provider decide that CASGEVY is right for you, your ATC will schedule an appointment for **blood stem cell collection** and any related appointments you might need, which you can learn about in the next steps in this brochure.



CASGEVY and family planning

Chemotherapy is needed before receiving CASGEVY. It's an important part of the process but can also affect your ability to have children. Talk to your healthcare team to discuss the **fertility preservation** options that may be available to you. Fertility preservation is a procedure that saves sperm, eggs, or reproductive tissue for possible use at a later date. For more information about chemotherapy, see [here](#).



Questions for your healthcare team

1. How long will I be away from home, work, or school at different points in the journey?
2. What support is available to me?
3. What are my insurance benefits, and what will I need to pay for?
4. What are my options for fertility preservation? What's involved?
5. How long will I need to use contraceptives?

Once a healthcare provider decides that CASGEVY is right for a patient, there are support services available for patients to enroll in. However, enrollment is not required to receive CASGEVY.



STEP 2 PREPARING FOR CELL COLLECTION

 **You will continue receiving transfusions**

CASGEVY[™] is a treatment that is made using your own blood stem cells. These are cells that can develop into **red blood cells**.

Before your healthcare team collects your blood stem cells, they'll want to make sure your body is ready. This includes continuing to get **red blood cell transfusions** (RBCTs) until your hemoglobin reaches a specific level that will prepare you for cell collection. Your healthcare provider will make adjustments as needed to get your body to that specific hemoglobin level before the next step can take place.

You may need to stop taking certain medications for at least 8 weeks during this step. Your healthcare provider will inform you if any updates need to be made to your medications.



Questions for your healthcare team

1. Are the RBCTs for this step different than the transfusions I'm already getting for my TDT?
2. Do I continue my regular schedule of TDT transfusions, or will my schedule need to change?
3. Should I make any changes to my diet or medications I take?



STEP 3 COLLECTING YOUR BLOOD STEM CELLS

 **Location of this step is determined by the healthcare provider**

 **Up to 7 days**

Once you've finished transfusions, you can begin the process of collecting your **blood stem cells**. Your blood stem cells are the cells used to make CASGEVY[™] specifically for you.

THE COLLECTION PROCESS HAS 2 PARTS:

1. **Moving your blood stem cells into the bloodstream, also called mobilization:**

Your healthcare team will give you a medicine that helps your blood stem cells move from your **bone marrow** to your blood so they can be collected. In the clinical study, mobilization happened in 2 stages:

- For the first 4 days, people received a medicine called granulocyte-colony stimulating factor (G-CSF)
- For the next 3 days, people received a medicine called plerixafor (in addition to G-CSF, which continued for 1-2 additional days)

2. **Blood stem cell collection, which may be called apheresis:**

A healthcare provider will use an intravenous, or IV, line to hook you up to a blood stem cell collection machine. This machine separates blood stem cells from your blood and then returns your blood to your body.

This step may happen more than once to collect enough blood stem cells to make your CASGEVY.



WHAT TO EXPECT

Your healthcare provider may recommend that you get a central line for collection.

- A central line is a tube that's placed in your vein. It makes it easier to draw blood over several days or weeks

Blood stem cell collections

In the clinical study, on average,* people required 1 cycle of blood stem cell collection.

- If more than 1 collection is needed, each collection will be separated by a minimum of 14 days and you will be able to return home during that time. This gives your body time to make new blood stem cells
- Your healthcare team can work with you to schedule these appointments

During this step, extra cells called "back-up cells" are also collected and stored at the ATC. These are not sent out for editing and are stored frozen at the center in case there are any issues in the treatment process. If CASGEVY can't be given to you for any reason or does not work in your body, your healthcare provider will put these back-up cells back into your body. If you are given back-up cells, you will not have any treatment benefit from CASGEVY.



Questions for your healthcare team

1. Are there any side effects from the mobilization medicine?
2. How long should I plan to be at the ATC?
3. Will I receive any other tests before my collection?
4. Can I continue my other beta thalassemia medications?

*This was measured as a median amount, which is the middle value of a group of numbers; half of the numbers are less than the median and half are higher.



STEP 4 MAKING YOUR CASGEVY[™]

 **You'll be at home while CASGEVY is being made at a lab**

 **5-6 months**

After your blood stem cells are collected, they will be carefully packaged and shipped to a lab. This is where CASGEVY will be made specifically for you using your own blood stem cells. You will return home until your treatment is ready.

Making your CASGEVY

- Your blood stem cells will be precisely edited using a technology called **CRISPR/Cas9**
 - CRISPR/Cas9 edits your stem cells so they can start making fetal **hemoglobin** again. Hemoglobin is the protein in red blood cells that helps carry oxygen to the rest of the body
 - Editing outside of the targeted gene was not observed in the modified blood stem cells of people living with TDT and healthy volunteers. The risk of editing outside of the targeted gene cannot be ruled out, due to differences in people's DNA. The impact of editing outside of the targeted gene is unknown
- Your edited stem cells will be tested to make sure they meet specific standards and are ready for your upcoming **infusion**



Your treatment

Throughout this process, your cells will be tracked using a unique code that's specific to you. This helps ensure that your cells—and only your cells—are used to make your CASGEVY.



WHAT TO EXPECT

- You can return home for the next 5-6 months while your CASGEVY is being made specifically for you
- People who want to preserve their fertility should discuss options with their healthcare provider before treatment
- You'll receive red blood cell transfusions during this time to maintain your hemoglobin above a certain level and your healthcare provider may have you stop taking certain medications before you receive chemotherapy
- You'll talk with your healthcare team about scheduling your CASGEVY infusion. Work with them to find a time that's best for your schedule
- While waiting for your CASGEVY treatment, you should start preparing for your upcoming stay at your ATC
 - Talk with your loved ones and discuss how they can help cover responsibilities you may have at home
 - Update anyone else who needs to know you will be away, such as your work or school



Questions for your healthcare team

1. Will I need any medications or treatments while I wait for my CASGEVY?
2. How is CASGEVY different from other treatment options?
3. How will I know when my CASGEVY is ready?



STEP 5 CHEMOTHERAPY, RECEIVING CASGEVY™, AND RECOVERY

 **At your ATC**

 **Approximately 7 weeks**

Once your CASGEVY is ready, you will travel to your Authorized Treatment Center (ATC) to undergo chemotherapy and receive your CASGEVY infusion.



WHAT TO EXPECT

Chemotherapy

- The first step at the ATC is undergoing chemotherapy. In the clinical study, this took 4 days. Chemotherapy clears stem cells out of the bone marrow to make room for your new CASGEVY blood stem cells
- The chemotherapy will cause your blood cells to fall to a very low level, so your healthcare providers will continue to monitor how you're feeling and allow you time to rest. Talk to your healthcare providers about other side effects of chemotherapy



Deciding on fertility preservation

It's important to discuss options for fertility preservation with your healthcare provider before going through chemotherapy, as chemotherapy may prevent you from becoming pregnant or fathering a child.

Questions for your healthcare team

1. Why do I need chemotherapy?
2. What can I do to prepare for chemotherapy and my CASGEVY infusion?
3. What side effects are chemotherapy or CASGEVY associated with?
4. Is there a diet I should follow before or after chemotherapy?
5. Will I experience hair loss from chemotherapy?
6. Can I continue the process if I become pregnant?

Receiving CASGEVY

- You will then receive CASGEVY as a one-time infusion through an IV into the vein
 - One or more vials of CASGEVY will be given into your vein over a short period of time. The number of vials will vary by patient

Recovery

- After the CASGEVY infusion, you will stay at the ATC so your healthcare provider can closely monitor your recovery
 - Your healthcare provider will decide when you can go home
- After receiving chemotherapy and CASGEVY, your immune system will need time to recover. Consider bringing personal items like photos, special blankets, or other keepsakes from home that are meaningful to you, as you may have limited interaction with loved ones



After CASGEVY infusion

Engraftment is the process by which blood stem cells received on transplant day are successfully accepted by the body and start to grow and make working blood cells in the body (or engraft).



Questions for your healthcare team

1. How long will my CASGEVY infusion take?
2. Will I feel anything with my CASGEVY infusion?
3. Can I eat or drink anything during or after my infusion?
4. How will I be monitored at the ATC?
5. When will I be able to see my family and friends after my treatment?
6. How long will I stay in the hospital?
7. Are there other treatments to stop after CASGEVY?
8. Will I have to stay in bed after my CASGEVY infusion or can I walk around?

IMPORTANT SAFETY INFORMATION

What are the possible or reasonably likely side effects of CASGEVY?

The most common side effects of CASGEVY include:

- Low levels of platelet cells, which may reduce the ability of blood to clot and may cause bleeding
- Low levels of white blood cells, which may make you more susceptible to infection

Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells). Tell your healthcare provider right away if you get any of the following symptoms:

- fever
- chills
- infections
- severe headache
- abnormal bruising
- prolonged bleeding
- bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.



STEP 6 AFTER TREATMENT

Once your healthcare provider determines you have recovered, they will tell you when you can go home. You will work with your healthcare team to come up with a long-term follow-up plan. This will include appointments with your healthcare provider and ATC to continue to monitor your health.



Monitor your health

Between visits, be sure to call your healthcare provider with any questions you may have and if you experience any side effects.



WHAT TO EXPECT

- Your ATC healthcare team will confirm how often they want to meet with you
- It's important to keep in mind that, after receiving CASGEVY[™], you will not be able to donate blood, organs, tissues, or cells at any point in the future



Questions for your healthcare team

1. How often will I have appointments to check my progress?
2. What can I expect after receiving CASGEVY?
3. What should I do if I experience side effects?
4. When can I go back to work, school, and other normal activities?
5. When can I see my friends and family?

PREPARING FOR THE ROAD AHEAD

Now that you know more about the treatment process, here are other ways to help feel prepared for what's next:

- **Create your support network:** Identify the people in your life who can help support you during the process. Your network could include your family, friends, and healthcare team
- **Plan for stays away from home:** You will need to be away from home, work, or school for periods of time. Think about who you may need to tell at your work or school. Ask what options for taking time off are available so you can focus on your treatment and your health

COMMUNICATION IS KEY

Often, the best way to find support is simply by asking. Think about a few important areas where you will need support during the treatment process. Then meet with your support network and let them know how they can help.



CONNECTING YOU TO THE JOURNEY AHEAD

Vertex Connects[™] is a program for people who have been prescribed a Vertex gene therapy, and their loved ones.

Support is here for you:

From the start of your treatment journey, your Vertex Connects Care Manager will be with you. They understand the CASGEVY[™] treatment process and have experience working with patients and families.

After enrolling* in Vertex Connects, your Care Manager will:

- Answer key questions about the treatment process and share useful guides to help you and your loved ones prepare for each step
- Keep in touch with your treatment center team to help coordinate the logistics of your treatment journey
- Connect in a way that works best for you—whether it's by email or phone
- Spend time getting to know you so they can provide meaningful support

*A completed Vertex Connects enrollment form is needed to participate in the program and determine eligibility for certain program offerings. Enrollment in Vertex Connects Patient Support is not required to receive Vertex gene therapy.

ADDITIONAL NOTES

Use this space to write down any notes from discussions you have with your healthcare provider.

GLOSSARY

There may be some terms in the treatment journey that are new to you. Knowing what they mean is important so you can feel more confident about the treatment journey. It can also help you have better conversations with your healthcare team.

Blood stem cells

Blood stem cells are a specific type of stem cell found in the bone marrow that can develop into either red blood cells, white blood cells, or platelets.

Blood stem cell collection, also known as **apheresis**
Process in which a portion of the blood is temporarily removed from the body to collect blood stem cells. After the cells are collected, the person's blood is returned to their body.

Bone marrow

The spongy part in the center of some bones where stem cells can develop into blood cells, such as red blood cells or white blood cells.

Chemotherapy

Chemotherapy is used to treat more conditions than cancer. In gene therapy, it's used to make room in your bone marrow to receive the edited stem cells.

CRISPR/Cas9

A type of gene-editing technology that can change DNA in order to treat diseases. CRISPR (cris-per) stands for clustered regularly interspaced short palindromic repeats.

Engraftment

Process by which blood stem cells received on transplant day are successfully accepted by the body and start to grow (or engraft) healthy blood cells in the body to help fight or treat disease.

Fertility preservation

A process that saves a person's eggs or sperm so they may have the option to have children in the future.

Gene therapy

Technique that adds, removes, or edits the genes inside cells. It may help manage or treat a genetic disease.

Hemoglobin

Protein in red blood cells that carries oxygen from the lungs to the rest of the body.

Infusion

The process that delivers a treatment into your body through a vein.

Mobilization

Process by which certain medicines are used to move stem cells from the bone marrow into the blood so they can be collected from the body.

Myeloablative conditioning

Myeloablative (my-eh-loh-blay-tiv) conditioning is a type of chemotherapy. It's used for a short time in people with TDT who are undergoing a bone marrow transplant (hematopoietic stem cell transplant). It helps remove stem cells in the bone marrow to create space for new stem cells to grow.

Red blood cell

A type of blood cell that carries oxygen throughout the body to the tissues and organs. They are round, flexible, and disc-shaped.

Red blood cell transfusion (RBCT)

A blood transfusion that helps increase the amount of donor red blood cells in your body.



**For information about
how CASGEVY™ works,
clinical study results,
and more,
visit [CASGEVY.com](https://casgevy.com).**

**Please see Important Safety Information
on page 5 and full Prescribing Information,
including Patient Information, for CASGEVY.**



This material was created by Vertex with insight and support from the beta thalassemia community.



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