Guide for Patients and Carers

Important Information About CASGEVY®▼ (exagamglogene autotemcel)

CASGEVY (exagamglogene autotemcel) is a one-time gene therapy that can be used to treat:

- People 12 years of age and older with beta thalassemia who need regular blood transfusions.
- People 12 years of age and older with sickle cell disease and frequent painful crises (called vaso-occlusive crises) who have the β^S/β^S, β^S/β^+ or β^S/β^0 genotype.

Carers: Please support the patient you are caring for in understanding this guide.

This Guide provides information on two important side effects of CASGEVY:

- Prolonged period of time after treatment with CASGEVY for the body to produce adequate levels of platelets (known as longer time to platelet engraftment). Platelets are the blood cells that stick together to stop bleeding. When platelet levels are inadequate, there is an increased risk of bleeding.

- The possibility that after treatment with CASGEVY neutrophils fail to re-establish in the body (known as neutrophil engraftment failure). Neutrophils are a type of white blood cell that protects the body from infections. A failure to re-establish these cells increases the risk of infections.

This Guide does not contain all the information about CASGEVY. Please read the Patient Information Leaflet and talk with your doctor for further information.

▼ **This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects that you, or the person you are caring for, experience from being treated with CASGEVY (see Section 5 of this Guide).**

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VERTEX

casgevy▼ (exagamglogene autotemcel)

1. About CASGEVY

CASGEVY is a one-time gene therapy. In the case of CASGEVY, a change is made in a specific gene that controls a special type of haemoglobin called fetal haemoglobin (HbF). This change increases the production of HbF. Having more HbF increases overall haemoglobin levels in the body and has been shown to improve the production and function of red blood cells in carrying oxygen through your body.

CASGEVY is made specifically for each patient, using the patient's own blood stem cells.

Glossary	
Stem cells	Special type of cell that can develop into many different cell types, such as blood cells
Blood stem cells	A type of stem cell found in your bone marrow that can develop into red blood cells, platelets, or white blood cells
Platelets	Blood cells that stick together to stop bleeding
White blood cells	Blood cells that are a part of the immune system. They are important for protecting the body from infection
Neutrophils	A type of white blood cell
Red blood cell	A type of blood cell that carries oxygen throughout the body

To produce CASGEVY for you, your blood stem cells are collected from you and are genetically changed outside of your body. The genetically changed cells are then given back to you through a haematopoietic (hee-MA-toh-poy-EH-tik) stem cell transplant, also called a bone marrow transplant. A haematopoietic stem cell transplant is a treatment that replaces unhealthy blood stem cells with the genetically changed healthy cells. Some of your original stem cells will not be genetically changed and will be stored as "rescue cells" in case there is a problem with your treatment.

Before treatment with CASGEVY, you will go through two pre-treatment stages.

- Stem Cell Mobilisation: In this stage, you will be given medicines that move the blood stem cells from the bone marrow into the blood stream so they can be more easily collected from the body via procedure called apheresis. Apheresis is a 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. It is possible that you may need to repeat this stage if not enough cells are collected the first time. The cells collected during mobilisation will be used to make CASGEVY which will be given to you after conditioning.
- Conditioning: In this stage, you will be given a conditioning medicine (a type of chemotherapy) as an infusion into a vein for a few days in the hospital. This will remove most of your blood stem cells that are not working properly from the bone marrow to create space for the genetically changed blood stem cells (CASGEVY) received on the transplant day to grow.

2. Important side effects

After being given CASGEVY, you will have fewer blood cells in your body until the genetically changed stem cells received on transplant day are successfully accepted by your body and begin to grow (or engraft). This means that, at first, you will have higher risk of bleeding (due to low platelets) or infection (due to low neutrophils) until these cells re-establish themselves.

While in the hospital, your doctor will monitor your blood cell counts, including your platelets and neutrophils (white blood cells), with regular blood tests. You will stay in the hospital until your neutrophils have returned to a level that enables you to fight infection.

There is a possibility that after treatment with CASGEVY neutrophils fail to re-establish in the body. If this happens, it may be necessary to return to your body your own untreated stem cells (rescue cells) that were collected and stored before you received CASGEVY. If this is the case, you will not receive any benefit from CASGEVY treatment.

Once you leave the hospital, your platelet levels may still not have returned to normal. There may be a prolonged period of time after treatment with CASGEVY for your body to produce adequate levels of platelets. Your doctor will continue to monitor your platelet counts with blood tests after you are discharged from the hospital. Until your platelets return to an adequate level, you will be at risk for bleeding. It is very important that you watch for any symptoms that could be a result of bleeding.

Some symptoms of bleeding are listed below. However, this list does not cover every symptom of bleeding.

Tell your doctor right away if you have any symptoms of bleeding, even if not listed here:

- Abnormal bruising
- Prolonged bleeding
- Severe headache
- Bleeding without injury such as:
  - Nosebleeds
  - Bleeding from gums
  - Blood in your urine, stool, or vomit
  - Coughing up blood

When you are leaving the hospital, your doctor will give you a Patient Alert Card. Keep this card with you at all times to remind you of the symptoms of bleeding, and show the card to all your doctors.

This Guide does not contain all the information about CASGEVY. Please read the Patient Information Leaflet and talk with your doctor for further information.

3. Other important information

As CASGEVY is a gene therapy, once you have been treated with CASGEVY, you should never donate blood, organs, tissues, or cells.

4. CASGEVY long-term study

As with all new treatments, there is limited information on the effects of CASGEVY over the long term. A study has therefore been set up to follow over a longer period of time patients who have received CASGEVY.

If you do take part in this study, you **will not** be required to undergo any additional tests, treatments or visits to the doctor beyond your routine tests, treatments, or visits. If you choose not to take part, **your choice will not affect the care that you receive**, and your doctor will continue to treat you in a way that is in your best medical interests. Please talk to the doctor who treated you with CASGEVY to find out more about the study.

5. Reporting side effects

If you, or the person you are caring for, experience any side effects after your treatment with CASGEVY, talk to your doctor or nurse. This includes any side effects, not just those addressed in this Guide.

You can also report side effects directly via the Yellow Card Scheme at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you are helping to provide more information on the safety of this treatment.

Any suspected adverse reactions to CASGEVY should also be reported to Vertex Pharmaceuticals (UK) Ltd on +44 (0) 800-028-2616 or at vertexmedicalinfo@vrtx.com.