CSL Behring

This educational material is provided by CSL Behring Ltd and is mandatory as a condition of the Marketing Authorisation in order to further minimise important selected risks.

Patient and Caregiver Guide

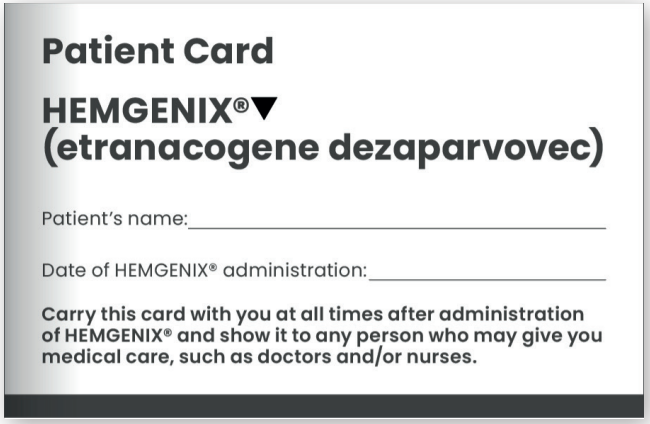
HEMGENIX®▼ (etranacogene dezaparvovec)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may experience.

Read this patient/caregiver guide carefully before you receive HEMGENIX® because it contains important information for you.

HEMGENIX® RMP Patient/Caregiver Guide
Version 1.0 - GBR-HGX-0020
Date of preparation: October 2023

In addition to this guide, your doctor will give you a Patient Card. Read it carefully and follow the instructions on it.



Patient Card

HEMGENIX®▼
(etranacogene dezaparvovec)

Patient's name:_____

Date of HEMGENIX® administration:_____

Carry this card with you at all times after administration of HEMGENIX® and show it to any person who may give you medical care, such as doctors and/or nurses.

Keep your Patient Card with you at all times and present it to any doctor or other healthcare professional you consult. The card contains important information for your safety related to the follow-up of this medication that you and healthcare professionals need to know before taking care of you.

What can you find in this guide?

1. What is HEMGENIX® and what is it used for?

HEMGENIX® is a gene therapy product that contains the active substance etranacogene dezaparvovec.

People with haemophilia B are born with an altered form of a gene needed to make factor IX, an essential protein required for blood to clot and stop any bleeding. People with haemophilia B have insufficient levels of factor IX and are prone to internal or external bleeding episodes.

HEMGENIX® is used for the treatment of severe and moderately severe haemophilia B (congenital factor IX deficiency) in adults who do not have current or past antibodies against factor IX protein, called factor IX inhibitors.

2. How does HEMGENIX® work?

The active substance in HEMGENIX® is based on a virus that does not cause disease in humans. This virus (also known as a vector) has been modified so that it cannot spread in the body but can deliver a copy of the factor IX gene into the liver cells. This allows the liver to produce the factor IX protein and raise the levels of working factor IX in the blood. This helps the blood to clot more normally and prevents or reduces bleeding episodes.

3. What you need to know before you are given HEMGENIX®

It is important that you fully understand the benefits and risks of HEMGENIX® treatment, what is known and not yet known about the long-term effects of this therapy, related to both safety and efficacy. Important information about HEMGENIX® treatment is provided in the sections that follow. Read it carefully and ask your doctor or nurse if you have further questions.

a. Liver health

BEFORE TREATMENT WITH HEMGENIX®

To decide if this therapy is suitable for you, your doctor will check your liver health before you start treatment with HEMGENIX® using:

- Blood tests to check the level of liver enzymes in your blood
- Liver ultrasound
- Elastography tests to check for scarring or thickening of your liver

AFTER TREATMENT WITH HEMGENIX®

After treatment with HEMGENIX®, your doctor will continue to check your health using blood tests. It is **important** that you **discuss the schedule for these blood tests** with your doctor so that they can be carried out as necessary.

HEMGENIX® will trigger a response within your immune system that could lead to increased levels of certain liver enzymes (transaminases) in your blood. This is called transaminitis. **Your doctor will regularly monitor your liver enzyme levels** to ensure that the therapy is working as it should:

In the first 3 months: At least once a week	**From month 4 up to 1 year:** Once every 3 months	**The second year:** Once every 6 months	**After the second year:** Once every year for at least 5 years

- **If you experience an increase in liver enzymes, you may have more frequent blood tests to check the levels of your liver enzymes, until they return to normal**
- **You may also need to take another medicine (e.g., corticosteroids) to manage these side effects**
- **You should inform your doctor about current use of corticosteroids or other immunosuppressants. If you cannot take corticosteroids, your doctor may recommend alternative medicines to manage problems with the liver**
- Your doctor may also perform additional tests to exclude other causes for the increase in your liver enzymes, if needed, in consultation with a doctor experienced in liver diseases

Both before and after treatment, it is recommended that you **avoid taking medication that can cause liver damage. Tell your doctor or nurse if you are taking, have recently taken, or might take any other medicines.** If you are taking medications that are known to damage the liver (hepatotoxic medication), your doctor may decide that you may need to stop this medication to be able to receive HEMGENIX®.

b. Abnormal clotting of blood (thromboembolic events)

As you have haemophilia B, you usually have a reduced risk for developing a blood clot (e.g., pulmonary thromboembolism or deep venous thrombosis [DVT]), due to the inborn deficiency in your blood clotting system.

Restoring factor IX activity may bring your risk of blood clots up to a level similar to that experienced by the general non-haemophiliac population.

If you have pre-existing risk factors for abnormal clotting, such as a history of heart disease, arteriosclerosis, hypertension, diabetes, or advanced age, the potential risk of having a blood clot may be higher.

Be aware of signs of abnormal clotting:

Symptoms of blood clots could include any of the following:

- Sudden chest pain
- Shortness of breath
- Sudden onset of muscle weakness
- Loss of sensation and/or balance
- Decreased alertness
- Difficulty in speaking
- Pain/tenderness in the leg
- Increased warmth and red or discoloured skin on the leg
- Swelling of one or both legs

If you have any of the mentioned symptoms of a blood clot:

Seek urgent medical attention

c. Risk of cancer potentially associated with HEMGENIX®

HEMGENIX® will insert into liver cells, and it may insert into the DNA of other body cells. The clinical relevance of this is unknown, but it may contribute to a risk of cancer. In clinical studies, no cancers due to HEMGENIX® were identified. You should therefore discuss this with your doctor.

If you are a patient with pre-existing risk factors for liver cancer, your doctor **will regularly (e.g., annually) monitor your long-term liver health for at least 5 years after HEMGENIX® administration** and perform the following tests:

- Annual liver ultrasound
- Annual blood test to check for increases in alpha-fetoprotein

Some risk factors for liver cancer are:
- Liver fibrosis (scarring and thickening of the liver)
- History of hepatitis B or hepatitis C
- Fatty liver (nonalcoholic fatty liver disease, or NAFLD)
- Excessive use of alcohol

In the event of cancer, your doctor may perform further tests to check if HEMGENIX® has inserted into the cell DNA.

d. Transmission of HEMGENIX®

The active substance in HEMGENIX® may temporarily be excreted through your blood, semen, breast milk, or body waste – a process called shedding.

To ensure that people without haemophilia B are not exposed to HEMGENIX® DNA through the shedding process in your body and/or semen, **you must not donate blood; semen; or organs, tissues and cells for transplantation after treatment with HEMGENIX®.**

After a male patient has been treated with HEMGENIX®, the patient and any female partner **must avoid pregnancy for 12 months.** You should use **effective contraception** (e.g., barrier contraception such as a condom or diaphragm). This is to minimise any risk of the factor IX gene from a father's HEMGENIX® treatment being transmitted to a child with unknown consequences. For the same reason, male patients must not donate semen. **Discuss with your doctor which methods of contraception are suitable.**

HEMGENIX® should not be used in women who are pregnant, and is not recommended in women who may become pregnant. HEMGENIX® should not be used during breast feeding.

e. Development of factor IX inhibitors

Neutralising antibodies against factor IX proteins, called factor IX inhibitors, may stop HEMGENIX® from working properly.

If your bleeds are not controlled or your bleeds return, your doctor may check your blood for these factor IX inhibitors.

f. Pre-existing immunity against the vector

Some people may have natural pre-existing "immunity" (antibodies) against adeno-associated virus (AAV) vectors used for gene therapy – this may stop the factor IX gene from being delivered effectively.

High pre-existing immunity against the vector may reduce the efficacy of HEMGENIX®.

Therefore, **you are expected to be assessed for neutralising anti-AAV5 antibodies before treatment with HEMGENIX®.**

g. Response to treatment

There is a possibility that not all patients will benefit from treatment with HEMGENIX®.

Patients who do not respond to HEMGENIX® may still experience the long-term risks as outlined in sections 3a-g.

HEMGENIX® will not be re-administered if you have not responded to treatment or if you have lost the response.

4. Long-term follow-up after administration of HEMGENIX®

The long-term efficacy and safety of HEMGENIX® are still unknown.

Therefore, after treatment with HEMGENIX®, **you will be expected to enrol in a follow-up study to help assess the long-term safety of the treatment for 15 years, how well it continues to work, and any side effects that may be linked to the treatment.**

You are encouraged to talk to your doctor for additional information about the follow-up study before treatment with HEMGENIX®.

5. What is the Patient Card for?

The HEMGENIX® Patient Card contains important safety information that you and any healthcare professional may need to know **after treatment with HEMGENIX®.**

As explained in this guide, certain recommendations must be followed for safe use of HEMGENIX®, and it is therefore essential to share this information with all healthcare professionals you may need to consult. This is the role of the Patient Card.


Patient Card

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(etranacogene dezaparvovec)

Patient's name:_____

Date of HEMGENIX® administration:_____

Carry this card with you at all times after administration of HEMGENIX® and show it to any person who may give you medical care, such as doctors and/or nurses.

- Your doctor should give you a HEMGENIX® Patient Card on the day of HEMGENIX® administration
- Carry the card with you at all times; you can keep it in your wallet or purse
- Show the Patient Card to any doctor or nurse whenever you have a medical appointment
- If you need to go to Accident and Emergency, show the card as soon as you arrive
- Tell your caregiver or anyone close to you about your treatment and show them the Patient Card, because they may notice side effects that you are not aware of

This card also reminds you of important information you need to know about significant risks of HEMGENIX®.

6. What should I do if I suspect an adverse event?

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the patient information leaflet or patient/caregiver guide. You can also report side effects directly to the MHRA via the Yellow Card Scheme. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, call 0800 731 6789 for free, Monday to Friday between 9am and 5pm (messages can be left outside these hours). When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.

Adverse events should also be reported to CSL Behring UK Ltd on 01444 447 405.

7. Additional information

This guide and other documents developed as part of the HEMGENIX® risk management plan can be downloaded at www.medicines.org.uk. The eMC website is managed and owned by Datapharm Communications Limited. CSL Behring UK Ltd publishes risk management materials on this independent website.

For more information, please refer to the HEMGENIX® Patient Information Leaflet, which is also available at www.medicines.org.uk.

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