CSL Behring

Important Safety Information

HEMGENIX® (etranacogene dezaparvovec)

Patient / Caregiver Guide

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HEMGENIX® RMP Patient/Caregiver Guide
Version 1.0
Approved by Saudi Food and Drug Authority on October /2024

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

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

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

What can you find in this patient/caregiver guide?

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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 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 below. 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 the status of your liver health before you start treatment with HEMGENIX® and perform:

- Blood tests to check the level of liver enzymes in your blood
- Liver ultrasound
- Elastography testing 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. 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 an increased level of certain liver enzymes (transaminases) in your blood 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:	From month 4 up to 1 year:	The second year:	After the second year:
At least once a week	Once every 3 months	Once every 6 months	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 the healthcare professional about current use of corticosteroids or other immunosuppressants. If you cannot take corticosteroids, the 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 medication 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 a patient with Haemophilia B, you usually have a reduced risk for developing a blood clot events (e.g. pulmonary thromboembolism or deep venous thrombosis), due to inborn deficiency in the 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.

In case you have preexisting risk factors for abnormal clotting , such as a history of cardiovascular or cardiometabolic disease, arteriosclerosis, hypertension, diabetes, or advanced age, the potential risk of thromboembolic events may be higher.

Be aware of signs of abnormal clotting:

Signs of abnormal clotting could be:

- 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 observe signs of abnormal clotting:

Consult your doctor immediately

c. Risk of malignancy potentially associated with HEMGENIX®

HEMGENIX® will insert into liver cells and it could possibly insert into the liver cell DNA or the DNA of other body cells. As a consequence, HEMGENIX® could contribute to a risk of cancer, such as liver cancer (hepatocellular carcinoma). Although there is no evidence of this in the clinical studies so far, this remains possible because of the nature of the medicine, which has a viral component. You should therefore discuss this with your doctor.

- If you are a patient with preexisting risk factors for hepatocellular carcinoma 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 and
  - Annual blood test to check for increases in alpha-fetoprotein.

Some risk factors for hepatocellular carcinoma are:

- liver fibrosis (scarring and thickening of the liver)
- history of Hepatitis B, Hepatitis C
- fatty liver (nonalcoholic fatty liver disease; NAFLD)
- excessive use of alcohol

- In the event of cancer, your doctor may take a sample of your cancer (biopsy) 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 bodily waste, a process called shedding.

To ensure that people without Haemophilia B are not exposed to HEMGENIX® DNA through 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 condom or diaphragm). This is to prevent the theoretical risk that the Factor IX gene from a father's HEMGENIX® treatment is 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® is not recommended in women who are pregnant or are able to become pregnant.

e. Development of FIX inhibitors

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

Your doctor may check your blood for these FIX inhibitors if your bleeds will not be controlled or return after you have been given HEMGENIX®.

f. Pre-existing immunity against the vector

Some people may have natural preexisting "immunity" (i.e., antibodies) against adeno-associated virus (AAV) vectors used for gene therapy – this may stop the genetic information being delivered effectively.

High preexisting immunity against the vector may reduce the efficacy of HEMGENIX®.

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

g. Response to treatment

There is a possibility that not all patients benefit from treatment with HEMGENIX®. Patients who do not respond are still exposed to long term risks.

There will be no plans to re-administer HEMGENIX® if you have not responded to treatment or if you have lost the response.

4 Long-term follow-up after administratio of HEMGENIX®

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 study 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®.

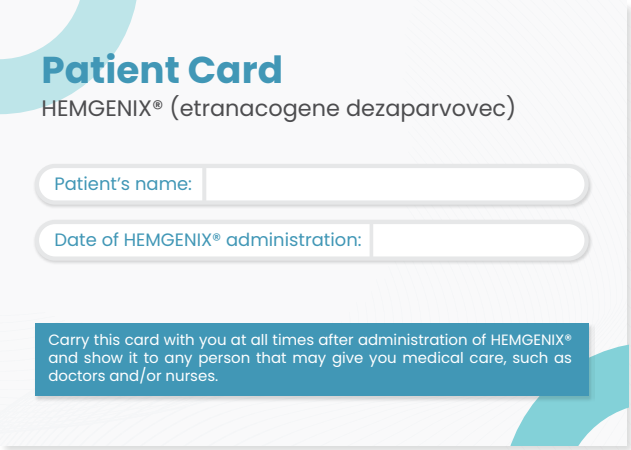
5 What is the Patient Card for?

The 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.

- Your doctor should give you a HEMGENIX® Patient Card on the day of HEMGENIX® administration
- Carry it with you at all times, you can keep it in your wallet or purse
- Show the Patient Card to any doctor or a nurse whenever you have a medical appointment
- If you need to go to an emergency room, show it 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 that may arise.



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

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this patient/caregiver guide. You can also report side effects directly using the reporting channels below By reporting side effects, you can help provide more information on the safety of this medicine.

National Pharmacovigilance Center (NPC) - Saudi Food and Drug Authority
SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa

CSL Behring:
Email: phvsa@cslbehring.com
Website: https://www.cslbehring.sa/en/report-adverse-event

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