PRESCRIBING INFORMATION: HEMGENIX®▼ (etranacogene dezaparvovec)

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each 10ml vial of etranacogene dezaparvovec contains 1 x 1013 genome copies (gc)/ml. **Indications:** Treatment of severe and moderately severe haemophilia B (congenital factor IX deficiency) in adult patients without a history of factor IX inhibitors. **Dosage and administration:** Single dose of 2 x 1013 gc/kg (2 mL/kg) as an intravenous infusion after dilution with sodium chloride (0.9%). Must not be administered as an intravenous push or bolus. HEMGENIX can be administered only once. Discontinuation of prophylaxis: Onset of effect from HEMGENIX treatment may occur within several weeks post-dose, therefore support with exogenous human Factor IX may be needed during the first weeks after HEMGENIX infusion. **Contraindications:** Hypersensitivity to the active substance or excipients, active infections, either acute or uncontrolled chronic, known advanced hepatic fibrosis, or cirrhosis. **Special warnings and special precautions for use:** Initiation of treatment: Prior to treatment assess for pre-existing neutralising anti-AAV5 antibodies, evaluate patient's liver transaminases and perform liver ultrasound and elastography (see SmPC for list of tests). Monitoring after treatment: Monitor factor IX activity (e.g., weekly for 3 months) and transaminases (e.g., weekly for at least 3 months). Consider corticosteroid taper if ALT raised (see SmPC). Infusion related reactions: closely monitor for infusion reactions (including hypersensitivity reactions and anaphylaxis) throughout and for at least 3 hours after infusion. Recommended infusion rate should be closely adhered to. Slow or stop infusion if infusion reaction suspected. Corticosteroid or antihistamine may be used for infusion reaction management. Thromboembolic events: Patients with pre-existing risk factors may be at higher risk (see SmPC). Contraceptive measures: Contraceptive measures needed for male patients or their female partners of childbearing potential. Blood/organ/cell/semen/tissue donation: Patients must not donate semen, blood, organs, tissues and cells for transplantation. Imunocompromised patients or those with active/controlled infections: clinical studies did not include immunocompromised patients. HIV positive patients: limited clinical data. FIX inhibitors: clinical studies did not include patients with FIX inhibitors. Elderly population: limited data in patients 65 years and older. Risk of malignancy because of vector integration: clinical relevance of individual integration events is not known. Patients with pre-existing risk factors for hepatocellular carcinoma should undergo regular monitoring (see SmPC). Contains 35.2 mg sodium per vial. **Fertility, pregnancy, and lactation:** not recommended in women of childbearing potential or during breastfeeding. No adverse impact on male fertility in animal studies observed. **Undesirable effects:** Headache, dizziness, nausea, fatigue, malaise, elevations in ALT, AST, CRP, creatine and bilirubin, influenza like illness, infusion related reactions (i.e., hypersensitivity, infusion site reaction, dizziness, eye pruritus, flushing, abdominal pain upper, urticaria, chest discomfort, pyrexia). Refer to the SmPC for full side effect profile and interactions. **Basic NHS Price:** £2.6 million **Legal Category:** POM **Marketing Authorisation number:** EU/1/22/1715/001, PLGB 15036/0160 **Further information available from:** CSL Behring UK Ltd, 4 Milton Road, Haywards Heath, West Sussex, RH16 1AH. Date text last revised: 13/03/2023. **PI Approval Code:** GBR-OTH-0838

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk/**.
Adverse events should also be reported to CSL Behring UK Ltd on **01444 447405**.

Reference:

1. HEMGENIX® (etranacogene dezaparvovec). Summary of product characteristics.

March 2024 GBR-HGX-0093

CSL Behring

A guide to adeno-associated virus type 5 neutralising antibodies (AAV5 NAbs) testing for

HEMGENIX®▼

(etranacogene dezaparvovec)

HEMGENIX® is a gene therapy medicinal product that expresses the human coagulation factor IX.

HEMGENIX® (etranacogene dezaparvovec) is indicated for the treatment of severe and moderately severe haemophilia B (congenital factor IX deficiency) in adult patients without a history of factor IX inhibitors.[1]

This medicinal product has been authorised under the conditional approval scheme. This means that further evidence on this medicinal product is awaited.[1]

Why should an AAV5 NAb test be performed?

- The HEMGENIX® UK Summary of Product Characteristics (SmPC) mandates AAV5 neutralising antibody testing before making a treatment decision.[1]
- Before administration of HEMGENIX®, a pre-existing anti-AAV5 neutralising antibody titre assessment should be performed.[1]
- Pre-existing anti-AAV5 neutralising antibodies above a titre of 1:678 (or equivalent) may impede transgene expression at the desired therapeutic levels and thus reduce the efficacy of HEMGENIX® therapy.[1]
- There is a lack of data in patients with anti-AAV5 neutralising antibodies above 1:678 (or equivalent). In one patient with a pre-existing anti-AAV5 neutralising antibody titre of 1:3212 in the clinical study, no factor IX expression was observed and restarting of exogenous factor IX prophylaxis was needed.[1]

AAV5 NAb Test by Precision for Medicine (PfM)

The AAV5 NAb Test performed by PfM measures anti-AAV5 neutralising antibodies in human serum.

Testing should take place as your patient considers treatment with gene therapy for haemophilia B and no less than one month before administration.

Order the **PfM AAV5 NAb* Test Kit** at aav5nabtest.co.uk

See inside for full prescribing information, or access the SmPC on:
https://www.medicines.org.uk/emc/product/14702/smpc

Adverse events should be reported. Reporting forms and information can be found at **https://yellowcard.mhra.gov.uk/**.
Adverse events should also be reported to CSL Behring UK Ltd on **01444 447405**.

AAV5 NAb TEST PROCESS

STEP 1 Order AAV5 NAb Test Kit

Order the **PfM AAV5 NAb Test Kit** at aav5nabtest.co.uk

To order your AAV5 NAb Test Kit from Precision for Medicine (PfM) please go to **aav5nabtest.co.uk** or scan this QR Code

- Log into your personal pre-registered account.
- If you have forgotten your account details, you can request a temporary password by contacting your local customer service support team.
- In parallel, do not forget to set up your MARKEN account on Maestro for the sample collection. Please note, your initial password will need to be updated within 72 hours.

AAV5 NAb Test Kit contains

VACUETTE® SS tube
2 Cryovials
1 Transfer pipette
1 Instructions for use
1 Biohazard bag
1 Cryosleeve

1 Form for return shipment (return shipment is organised by MARKEN)
1 Return shipper (Styrofoam box and outer shipping container)

All kit components can be stored at 4 °C to 25 °C until ready for use.

Materials that may be required but are not provided: needle, tube adapter, alcohol swab, bandage, gloves, gauze, tourniquet.

Do not use after expiry date printed on label

Once you have received the AAV5 NAb Test Kit, do not discard the outer cardboard shipping container, as it will be used for the transportation of the blood samples to the laboratory that performs the AAV5 NAb Test.

STEP 2 Complete the AAV5 NAb Test Requisition Form

- Download the AAV5 NAb Test Requisition Form at **aav5nabtest.co.uk**
- Fill out the form online, and once complete, print it off – **don't forget to sign it.**
- Fill in the ID stickers with the PfM-generated Patient ID and the collection date, and attach them to the printed form.
- Place the form into the bag provided with the AAV5 NAb Test Kit.
- The AAV5 NAb Test Requisition Form should be sent back together with the blood sample to PfM.
- Refer to Steps 3 and 4 for blood sample collection and shipment.

Specimens returned without a completed and signed AAV5 NAb Test Requisition Form cannot be tested until patient and specimen identities are verified. This may potentially result in testing and treatment delays.

STEP 3 In clinic: Collect test sample via blood draw

When collecting samples, please refer to the full instructions for use in the AAV5 Nab Test Kit you received.

FILL SAMPLE TUBE

- Label VACUETTE® SS tube and 2 cryovials with PfM patient ID (as stated on the AAV5 NAb Test Requisition Form) and date of collection.
- Record date (YYYY-MM-DD) and time of collection (24-hour clock, HH:MM) of the sample on the AAV NAb Test Requisition Form.
- Completely fill sample tube and gently invert tube 5–10 times.
- Transport the tube, the AAV5 NAb Test Requisition Form, and the collection kit– **including the outer cardboard shipping container**–to your corresponding laboratory.

STEP 4 In the laboratory: Prepare for shipment

SET AND CENTRIFUGE

- Upon reception of the tubes, allow blood to clot in an upright position for a minimum of 30 minutes.
- Centrifuge at a relative centrifugal force (rcf) of 1800 g for 10 minutes at 15 °C to 25 °C.

TRANSFER TO CRYOVIALS

- Using the transfer pipette, transfer serum from the SS tube equally into the 2 cryovials.
- Discard the SS tube in an appropriate biohazard container or in accordance with local procedure.

FREEZE AND SHIP

Both components of the return shipper must be used: Styrofoam box AND outer cardboard shipping container.

- Freeze samples at –70 °C or lower.
- The time from specimen collection to freezing should not exceed 2 hours.
- Contact the logistics partner, MARKEN, at least 48 hours ahead of your desired shipment collection time. For detailed shipping instructions, refer to your MARKEN starter kit or go to **www.precisionmedicinelab.com/markenshippinginstructions**
- On the day of shipment, place the cryovials into the cryosleeves, place the cryosleeves into the biohazard bag, and seal the biohazard bag.
- Place the completed and signed AAV5 NAb Test Requisition Form into the labelling pouch on the biohazard bag. Place the biohazard bag into the return shipper with dry ice provided by the courier driver.
- Once the shipping box is closed, attach the MARKEN transportation documents (house airway bill [HAWB] and pro forma invoice) provided by the driver.

Always use ONE sample per box. If you wish to return multiple samples, order the corresponding number of transports and use the provided kit Styrofoam box and outer carton box for EACH patient sample.

STEP 5 Review test results and discuss next steps

REVIEW TEST RESULTS

- AAV5 NAb Test results will be available approximately 3 weeks after shipment of serum samples at **aav5nabtest.co.uk**
- You will be notified by email when results are available for your patient.
- Your practice will receive a report providing the AAV5 NAb Test results.
- Test results are reported as AAV5 NAb titre or 'NO RESULT'. A reason will be provided if there is 'NO RESULT'.
- In certain circumstances, there may be a need for retesting.

SUPPORT FOR YOU

Precision for Medicine (PfM) provides you with their full expertise to answer questions about the **PfM AAV5 NAb Test Kit.** If you have any questions or problems with the AAV5 NAb Test Kit, please contact your local PfM customer service team:

- Through the form available at: **https://www.precisionmedicinelab.com/contact**
- By sending an email to: **CS-UK@precisionmedicinelab.com**
- Or calling this freephone number: **+44 80 8258 6822**

ARRANGING SHIPMENT OF SAMPLES

The samples will be transported to PfM by the logistics partner, MARKEN.

Organise sample collection with MARKEN here:

https://online.marken.com

For detailed shipping instructions, please refer to:

www.precisionmedicinelab.com/markenshippinginstructions

CSL Behring Medical Information Contact: **medinfo@cslbehring.com**