FIRST GENE THERAPY FOR HAEMOPHILIA B[1,2]
NOW REIMBURSED AND WITH 36-MONTH DATA

STEP INTO A WORLD WHERE LASTING ELEVATED FACTOR IX LEVELS MAY BE POSSIBLE[1,2]

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.

Click here for prescribing information.

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

Intended for UK Healthcare Professionals Only.

The image is used for illustrative purposes only and does not represent actual patients.

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HEMGENIX® IS THE FIRST APPROVED GENE THERAPY FOR HAEMOPHILIA B IN THE UK[2]

WHAT IS HEMGENIX®?

HEMGENIX® is an ***in vivo* gene therapy** that consists of a non-replicating recombinant **AAV5**, containing the ***F9* gene variant encoding the gain-of-function Padua variant of the human FIX protein**, under the control of a liver-specific promoter.[1,3]

It is designed to target the root cause of haemophilia B by introducing a functional copy of the *F9* gene to compensate for the *F9* mutation.[1]

The modified *F9* gene encoding the highly active FIX Padua protein variant is **shown to generate 5–8 times higher mean endogenous FIX activity** than the more common wild-type FIX protein.[4]

After years of scientific research and clinical study, gene therapy with HEMGENIX® has arrived

AAV5, adeno-associated viral vector serotype 5; FIX, factor IX.

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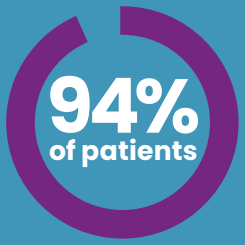
HEMGENIX® IS A ONE-TIME INFUSION

THAT OFFERS THE POTENTIAL FOR LONG-TERM BLEED PROTECTION, EVEN IN NAb-POSITIVE PATIENTS*[1,2]



(51/54) remained prophylaxis free at 3 years†[2]

38.6%

mean FIX activity sustained at 3 years‡[2]

ABR reduction in all bleeds during months 7–36 post-treatment compared with the 6-month lead-in period§[2]

HEMGENIX® is clinically effective even in eligible patients with pre-existing AAV5 NAbs (up to a NAb titre of 1:898 or equivalent)*[1,5]

Ongoing pivotal Phase 3 study; total of N=54 patients aged 19 to 75 years at enrolment with moderately severe or severe haemophilia B (FIX activity ≤2%) completed a 6-month observational lead-in period with standard-of-care routine FIX prophylaxis, after which patients received a single intravenous dose of HEMGENIX®. Post-treatment follow-up visits occurred regularly; 53/54 patients completed ≥18 months of follow-up. Study is ongoing to 5 years.[1]

*Patients with pre-existing anti-AAV5 neutralising antibodies (NAbs) were included in the HOPE-B clinical study. There is limited data in patients with NAbs above 1:678.[1,2]

†51 patients remained free of previous continuous routine FIX prophylaxis through to month 36 post-treatment. 1 participant lacked efficacy (highest AAV5 NAb titre of 1:3212). 1 participant received a 10% partial dose of treatment and did not discontinue prophylaxis. 1 participant eventually had his FIX levels decline to <5%; his bleeding phenotype returned, and he resumed prophylaxis per protocol at month 30 post-treatment.[2]

‡The mean ± SD (median; range) endogenous FIX activity level (i.e., in the absence of exogenous FIX exposure) of participants was 38.6 IU/dL ± 17.8 (36.0; 4.8–80.3, n=48) at year 3 post-treatment.[2]

§ABR for all types of bleeds after stable FIX expression decreased from a mean of 4.17 for the lead-in period (all patients were under stable prophylaxis) to a mean of 1.52 (one-sided *P*=0.0004) in months 7–36 post-dose.[2]

AAV5, adeno-associated viral vector serotype 5; ABR, annualised bleeding rate; FIX, factor IX; NAb, neutralising antibody; SD, standard deviation.

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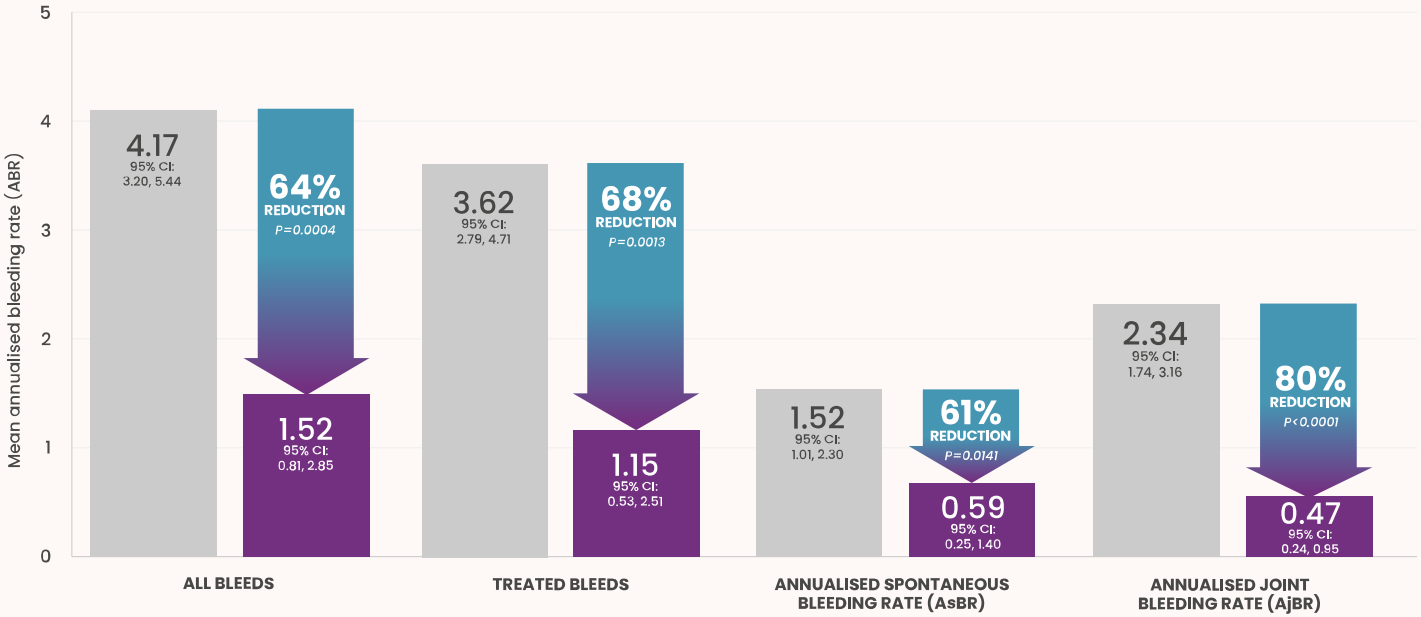
SUPERIOR BLEED PROTECTION AT MONTH 36

VERSUS LEAD-IN FIX PROPHYLAXIS[6]

64% REDUCTION IN ABR SEEN AT 18 MONTHS WAS SUSTAINED FOR 3 YEARS

VERSUS STABLE PROPHYLAXIS IN 6-MONTH LEAD-IN PERIOD
(1.52 VS. 4.17; *P*=0.0004)*[2]

Annualised bleeding rate across all types (n=54 patients)[6]



63% of patients (34/54) reported zero bleeds† in the 7–18 month period following a one-time infusion of HEMGENIX®, which **decreased to 42.6% of patients (23/54) at 36 months**[6]

*Mean ABR for all bleeds during months 7–36 post-treatment was significantly reduced by 64% (mean ABR 1.52) compared with the ≥6-month lead-in period (mean ABR 4.17; *P*=0.0004). Total number of bleeds (all types) was 136 during the ≥6-month lead-in period and decreased to 55 during year 1, 48 during year 2, and 37 during year 3 post-treatment. Median (range) bleeds per participant decreased from 2.0 (0–10) during the lead-in period and remained stable to 0.0 (0–4) during year 1, 0.0 (0–10) during year 2, and 0.0 (0–8) during year 3. Superior bleeding protection was in line with the level of transgene-derived endogenous FIX expression.[2]

†All types of bleeds: spontaneous; traumatic; FIX treated or not.

ABR, annualised bleeding rate; AjBR, annualised joint bleeding rate; AsBR, annualised spontaneous bleeding rate; CI, confidence interval; FIX, factor IX.

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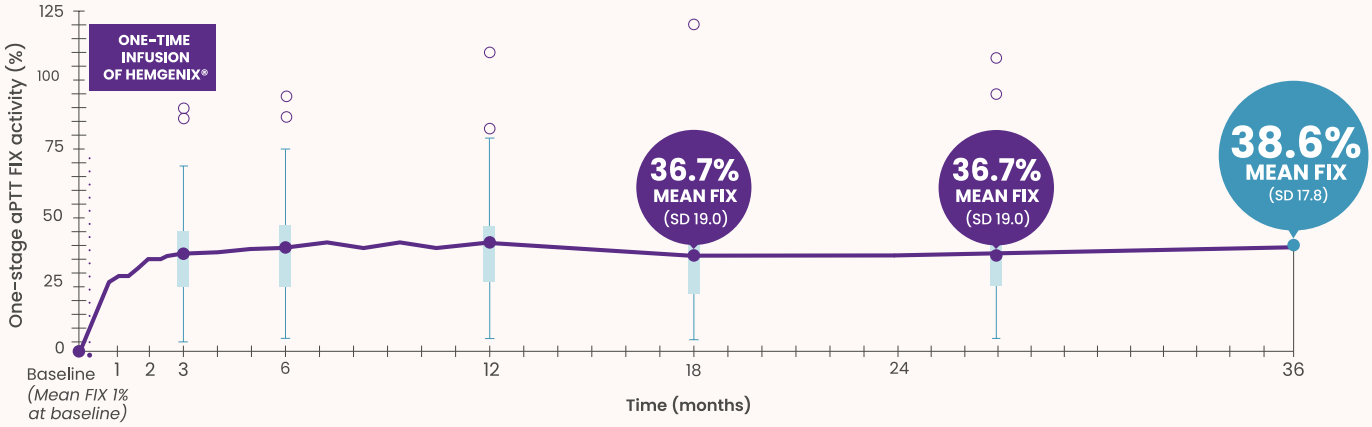
ELEVATED AND SUSTAINED FIX LEVELS FOR 3 YEARS

AFTER HEMGENIX® INFUSION[1,2,7,8]

FIX activity was sustained over 3 years after dosing[2]



At 3 years post administration, mean FIX activity was 38.6% (n=48; SD 17.8), sustained from 36.7% at 2 years (n=50; SD 19.0).*[2]

No clinically meaningful correlation was identified between a subject's AAV5 NAb titre at baseline (up to a titre of 1:700) and their FIX activity at month 36 postdose.[6]

O data outliers.

*Year 1, 41.5 IU/dL ± 21.7 (39.9; 5.9–113, n=50); pharmacodynamic profile was not significantly different in participants with AA5 NAb undetected or titre ≤1:678.[2]

This graph includes the full analysis set (FAS) of 54 patients. The FAS included 1 patient who received only 10% of the planned dose and 1 patient who did not respond to treatment (pre-existing AAV5 NAb titre of 1:3212).[1]

AAV5, adeno-associated viral vector serotype 5; aPTT, activated partial thromboplastin time; FAS, full analysis set; FIX, factor IX; NAb, neutralising antibody; SD, standard deviation.

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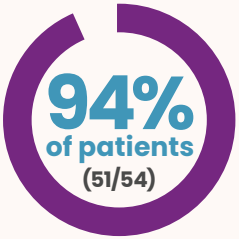
MAJORITY OF PATIENTS REMAINED FREE

OF PROPHYLAXIS AT 3 YEARS WITH HEMGENIX®[2]



DISCONTINUED ROUTINE FIX PROPHYLAXIS

and remained prophylaxis free at 3 years[2,6]

- 1 participant lacked efficacy; he had the highest AAV5 NAb titre of 1:3212 in the clinical trial
- 1 participant who received a 10% partial dose of treatment did not discontinue prophylaxis
- 1 participant eventually had his FIX levels decline to <5%; his bleeding phenotype returned, and he resumed prophylaxis per protocol at month 30 post-treatment

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IN OVERALL MEAN ANNUALISED FIX CONSUMPTION

over 3 years post-treatment compared to the ≥6-month lead-in period (*P*<0.0001)[2]

AAV5, adeno-associated viral vector serotype 5; FIX, factor IX; NAb, neutralising antibody.

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PATIENTS EXPERIENCED SIGNIFICANT IMPROVEMENTS IN OVERALL QUALITY OF LIFE[6]

Following treatment with HEMGENIX®, patients experienced:

SIGNIFICANT IMPROVEMENTS in patient-reported outcomes using the Haem-A-QoL score[6]

- In the domains of feelings, treatment, work/school, and future up to month 36 (P<0.0001) compared with the ≥6-month lead-in period[6]

OBSERVED IMPROVEMENTS IN EQ-5D-5L SCORES between months 12–36 post-treatment compared with the ≥6-month lead-in period[6]

- However, these differences were not statistically significant (P=0.0395)[6]

EQ-5D-5L, EuroQol 5-Dimension 5-Level; Haem-A-QoL, Haemophilia Quality of Life Questionnaire for Adults.

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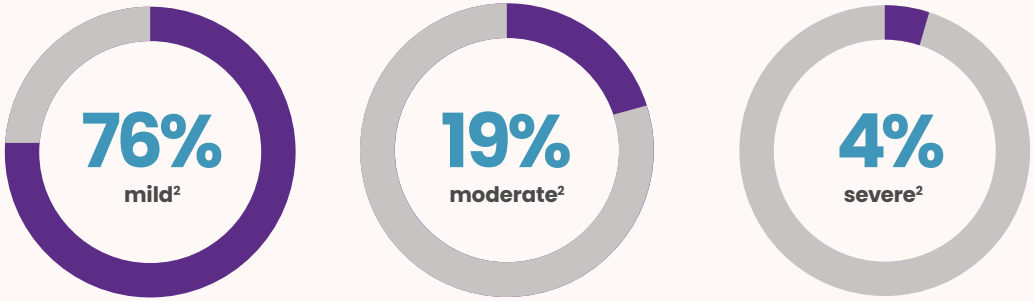
AT 3 YEARS, THERE WERE NO SERIOUS ADVERSE EVENTS

RELATED TO TREATMENT WITH HEMGENIX®[2]

DURING THE 3 YEARS POST-DOSE, ALL PARTICIPANTS EXPERIENCED AT LEAST 1 TREATMENT-EMERGENT ADVERSE EVENT (TEAE)[2]

Most TEAEs were:



Almost all TEAEs occurred during the first 6 months (95%).[2]

The most common AE was an increase in alanine aminotransferase (ALT), for which 9 (16.7%) participants received supportive care with reactive corticosteroids for a mean duration of 81.4 days (SD: 28.6; range: 51–130 days).[2]

There were no serious AEs related to treatment.[2]

No new deaths, no new hepatocellular carcinoma (HCC), and no late treatment-related ALT elevations or thromboembolic events were reported.[2]

A serious AE of HCC and a death were reported previously before year 2 and determined to be unrelated to treatment.[2]

AE, adverse event; ALT, alanine aminotransferase; HCC, hepatocellular carcinoma; SD, standard deviation; TEAE, treatment-emergent adverse event.

IMPORTANT SAFETY CONSIDERATIONS

WITH HEMGENIX®

Transient liver enzyme elevation[1,6]

All treatment-related ALT elevations were non-serious and resolved with a short course of corticosteroid treatment.

In the clinical Phase 2b and Phase 3 (HOPE-B) studies, ALT elevations occurred in 13/57 (22.8%) patients:

- Nine of the 13 patients with ALT elevations received a tapered course of corticosteroid. The mean corticosteroid treatment duration for those patients was 81.4 (± SD 28.6) days
- All treatment-emergent adverse events of elevated ALTs were non-serious and resolved within 3 to 127 days
- No corticosteroid-related adverse events were reported
- Prophylactic steroids to prevent ALT elevation were not part of the protocol

Patients should be monitored weekly for liver enzyme elevations in the first 3 months following HEMGENIX® administration.

Long-term liver health[1,2]

- A liver health assessment is required prior to the administration of HEMGENIX®
- There was one case of hepatocellular carcinoma (HCC) reported during the study. The event was assessed and unrelated to HEMGENIX® administration. Patients with pre-existing risk factors for HCC (such as hepatic fibrosis, hepatitis C or B disease, non-alcoholic fatty liver disease) should undergo regular liver ultrasound screenings and should be regularly monitored
- It is recommended that patients receive regular abdominal ultrasound screenings and are regularly monitored (e.g., annually) for alpha fetoprotein (AFP) elevations in the 5 years following HEMGENIX® administration (and at least 5 years for those with pre-existing risk factors for HCC)
- For additional safety considerations with regards to the potential risks of hepatotoxicity, thromboembolic events, malignancy as a result of vector integration, germline and horizontal transmission of HEMGENIX®, and development of FIX inhibitors, please refer to the HEMGENIX® SmPC

Contraindications[1]

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SmPC
- Active infections, either acute or uncontrolled chronic
- Patients with known advanced hepatic fibrosis, or cirrhosis

Patient considerations[1]

- Male patients should be informed on the need for contraceptive measures for them or their female partners of childbearing potential
- Patients treated with HEMGENIX® must not donate blood, organs, tissues, and cells for transplantation (patients will be provided with a patient card)
- Use in immunocompromised patients is based on healthcare professional's judgement
- Patients are expected to be enrolled in a follow-up study for 15 years

Data up to March 2023.

AFP, alpha fetoprotein; ALT, alanine aminotransferase; FIX, factor IX; HCC, hepatocellular carcinoma; SD, standard deviation.

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HEMGENIX® PROVIDES A STRAIGHTFORWARD TREATMENT JOURNEY FOR A BROAD RANGE OF APPROPRIATE PATIENTS[1]

WHAT HAPPENS AFTER A PATIENT IS TREATED WITH HEMGENIX®?

Long-term monitoring is recommended to monitor the patient's liver enzymes and FIX activity.[1]

These follow-up requirements will decrease over time, depending on the patient's FIX levels, their stability, and any evidence of bleeds.[1]

LOW REACTIVE STEROID USE REPORTED DURING FOLLOW-UP

LOW REACTIVE STEROID USE

Corticosteroids were used to treat patients with elevations in liver transaminases:

- **16.7% of patients** (9/54) received and discontinued corticosteroids†[6]
- For a mean (SD) duration of **81.4 (28.6) days** (range 51–130 days)†[2,6]

*In patients with FIX activity >5 IU/dL; consider more frequent monitoring in patients with FIX activity levels ≤5 IU/dL and consider the stability of FIX levels and evidence of bleeding.[1]

†Safety population. All treatment-emergent ALT increases were non-serious and resolved spontaneously or with a short course of corticosteroid treatment. Prophylactic corticosteroids to prevent ALT elevation are not required.[1,6]

ALT, alanine aminotransferase; FIX, factor IX; SD, standard deviation.

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WHAT COULD YOUR PATIENT'S HEMGENIX® JOURNEY LOOK LIKE?

1 PATIENT COUNSELLING AND SHARED DECISION-MAKING

Proactively speak to your appropriate patients about how gene therapy may help address urgent unmet need. For all other patients, continue ongoing discussions about gene therapy, as a patient's circumstances can change.

2 ASSESS PATIENT ELIGIBILITY[1]

Health screening tests are required to determine eligibility (e.g., ultrasound, elastography, bloodwork to evaluate liver health).

3 PRIOR TO INFUSION WITH HEMGENIX®[1]

Complete the Patient Treatment Form, including patient's weight and date of infusion. Before prescribing and administering HEMGENIX®, ensure the patient's eligibility and that the required screening tests are completed.

4 WHAT TO EXPECT ON INFUSION DAY[1]

HEMGENIX® is a one-time dose that takes around 1–2 hours to administer.

5 EXPECTATIONS AROUND FOLLOW-UP MONITORING REQUIREMENTS[1]

The follow-up monitoring requirements for patients decrease over time. Patients are expected to enrol in the follow-up study, in which their progress will be monitored for 15 years.

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