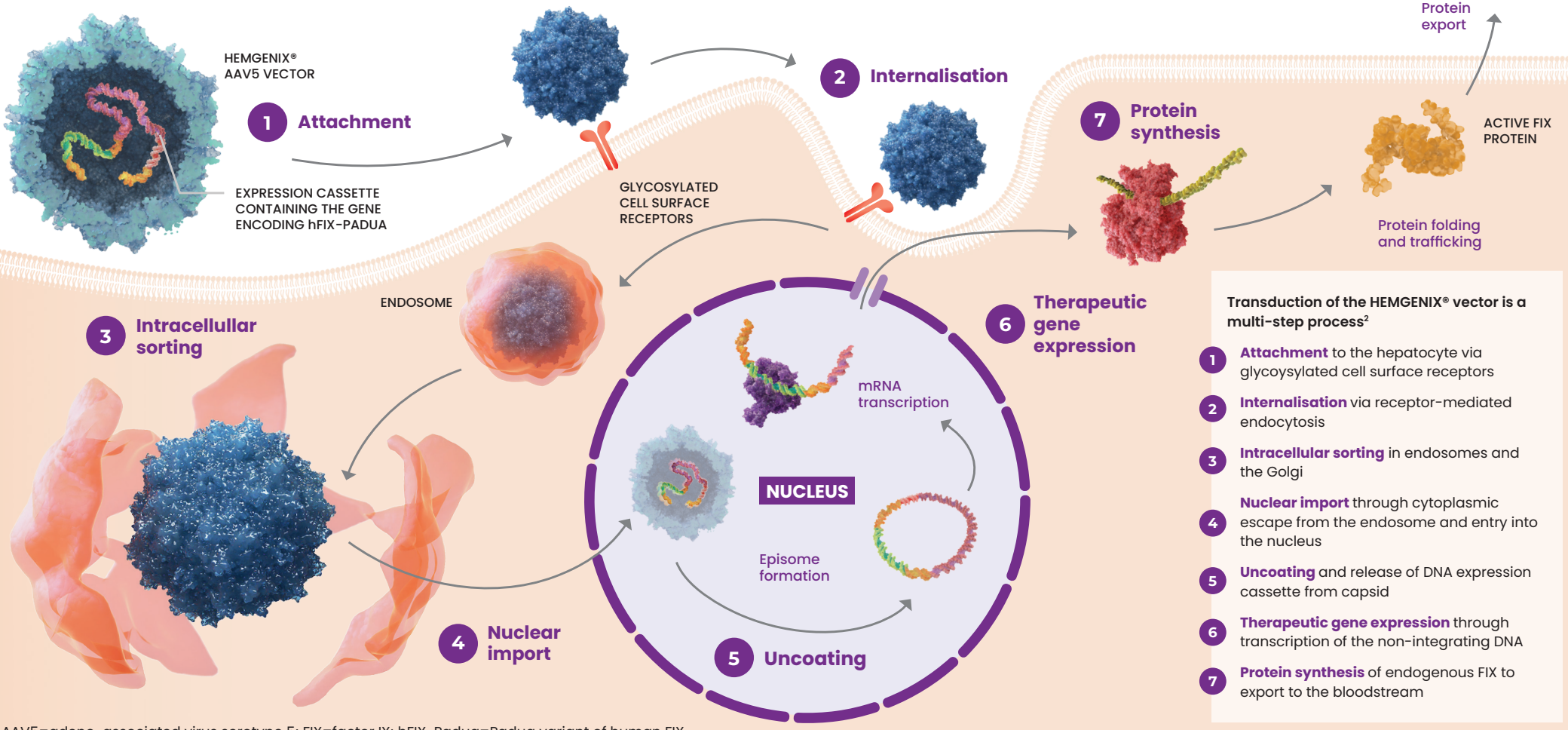
HEMGENIX®
etranacogene dezaparvovec

Mechanism of Action in Haemophilia B

HEMGENIX® is a gene therapy that uses a recombinant AAV5 vector to deliver a functional copy of the *F9* gene to the hepatocytes of eligible adults with severe or moderately severe haemophilia B. The vector is specifically designed to follow a multi-step process of *in vivo*, liver-directed gene transfer with the goal of achieving elevated and sustained endogenous expression of functional factor IX through a single IV administration.[1,2]



Transduction of the HEMGENIX® vector is a multi-step process[2]

1. **Attachment** to the hepatocyte via glycoysylated cell surface receptors
2. **Internalisation** via receptor-mediated endocytosis
3. **Intracellular sorting** in endosomes and the Golgi
4. **Nuclear import** through cytoplasmic escape from the endosome and entry into the nucleus
5. **Uncoating** and release of DNA expression cassette from capsid
6. **Therapeutic gene expression** through transcription of the non-integrating DNA
7. **Protein synthesis** of endogenous FIX to export to the bloodstream

AAV5=adeno-associated virus serotype 5; FIX=factor IX; hFIX-Padua=Padua variant of human FIX

1. HEMGENIX® (etranacogene dezaparvovec). Summary of product characteristics.
2. Wang D, et al. *Nat Rev Drug Discov.* 2019;18(5):358-378.

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Prescribing Information

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 10^{13} 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 10^{13} 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. Immunocompromised 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 be reported to CSL Behring UK Ltd on 01444 447405.

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