BlueCross BlueShield Nebraska

# HEMOPHILIA B GENE THERAPY (PREAUTHORIZATION REQUIRED)

X.209

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## POLICY

**Target Agents:**

**Hemgenix®** (etranacogene-dezaparvovec-drlb) is FDA approved: For the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who: currently use Factor IX prophylaxis therapy, OR have current or historical life-threatening hemorrhage, OR have repeated, serious spontaneous bleeding episodes.

| Brand (generic) | J-Code | Multisource Code | Quantity Limit (per day or as listed) |
|---|---|---|---|
| **Hemgenix (etranacogene-dezaparvovec-drlb)** | | | |
| | | M, N, O, or Y | 1 treatment per lifetime |
| | | | |

**Initial Evaluation**

I. Target Agent(s) may be considered **medically necessary** when **ALL** the following are met:

A. The patient has a diagnosis of congenital hemophilia B (also known as Factor IX deficiency, Christmas disease) **AND**

B. **ONE** of the following:

1. The patient's sex is male **OR**

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patient's sex (medical records required) **AND**

C. Patient is 18 years old or over **AND**

D. The patient has been screened for Factor IX inhibitor titers **AND ONE** of the following: (medical records required)

1. The patient tested negative for Factor IX inhibitor titers on the initial screening **OR**

2. **BOTH** of the following:

a. The patient tested positive for Factor IX inhibitors on the initial screening **AND**

b. The patient tested negative for Factor IX inhibitors within 2 weeks of initial screening

**AND**

E. **ONE** of the following: (medical records required)

1. The patient is on prophylactic therapy with a Factor IX agent (e.g., AlphaNine SD, Alprolix, BeneFIX,

Idelvion, Ixintiy, Mononine, Profilnine SD, Rebinyn, Rixubis) **OR**

2. The patient has current or historical life-threatening hemorrhage **OR**

3. The patient has had repeated, serious spontaneous bleeding episodes

**AND**

F. The prescriber has completed the following assessments:

1. Liver enzyme testing (i.e., alanine aminotransferase [ALT], aspartate

2. Hepatic ultrasound and elastography **AND**

3. If the patient has sustained liver enzyme elevations and/or radiological liver abnormalities, the prescriber has considered consultation with a specialist (i.e., hepatologist) **AND**

G. The patient has **NOT** had any previous gene therapy (including requested agent).

**Length of Approval: 1 per lifetime**

## Dates

Original Effective
**03-01-2023**
Last Review
**11-06-2024**
Next Review
**11-08-2025**

## CLINICAL RATIONALE

Hemophilia B, also called Factor IX (FIX) deficiency or Christmas disease, is a genetic disorder caused by missing or defective Factor IX, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation.(2)

The main goal of any therapy is to completely prevent bleeding. The current World Hemophilia Federation Guidelines for the Management of Hemophilia state:(3)

- Both virus-inactivated plasma-derived and recombinant clotting factor concentrates (CFCs), as well as other hemostasis products when appropriate can be used for treatment of bleeding and prophylaxis in people with hemophilia
- Prophylaxis is the standard of care for people with severe hemophilia, and for some people with moderate hemophilia or for those with a severe bleeding phenotype and/or a high risk of spontaneous life-threatening bleeding
- Episodic CFC replacement should not be considered a long-term option for the management of hemophilia as it does not alter its natural history of spontaneous bleeding and related complications

need for intravenous administration, short half-life, risk of inhibitor formation)
- The development of gene therapies for hemophilia has advanced significantly, with product registration likely in the near future
- Gene therapy should make it possible or some people with hemophilia to aspire to and attain much better health outcomes and quality of life than that attainable with currently available hemophilia therapies
- Given the ongoing advances transforming the hemophilia treatment landscape, it is important to establish systems to constantly monitor developments in emerging and gene therapies for hemophilia and make them available as soon as possible following approval by regulatory authorities

Adeno-associated virus (AAV)- mediated gene therapy is increasingly recognized for its potential to treat many monogenic diseases, including hemophilia A and B, by means of delivery of complementary DNA encoding functional Factor VIII or Factor IX proteins, respectively.(7)

Numerous human Phase 1/2 clinical trials for hemophilia B and A have been conducted over the past decade. These trials have incorporated modifications of promoters, transgenes, and adeno-associated virus (AAV) vector serotypes, resulting in varying adverse events and levels of Factor IX or Factor VIII. More Phase 1/ 2 trials are in planning stages, including with different transgene delivery systems (e.g., lentiviral vectors). Further, four Phase 3 trials, 2 each in Hemophilia B and A are underway. While the initial results offer the prospect of a potential cure for hemophilia, many questions regarding efficacy and safety remain.(8)

Most ongoing trials have shown transient hepatic enzyme elevations, signifying toxicity, in at least a subset of clinical trial participants. The mechanisms behind this toxicity are not fully understood, but include:(8)

- An immune response to vector capsid
- Possible direct cellular toxicity due to stress from catabolizing the AAV capsid
- A cellular stress response due to high transgene protein synthesis burden and/or
- Hepatotoxicity resulting from interaction of vector and co-administered potentially hepatotoxic medications, e.g., efavirenz

While the mechanisms are not all understood, these adverse events support the need to counsel patients receiving gene therapy to avoid potentially hepatotoxic therapies such as within HAART and support the

Hemgenix (etranacogene dezaparvovec-drlb) is an adeno-associated virus serotype 5(AAV5) based gene therapy designed to deliver a copy of a gene encoding the Padua variant (variant R338L) of human coagulation Factor IX (hFIX-Padua). It is a one-time infusion of the highly active Padua variant of the gene for Factor IX into cells in the liver, resulting in cell transduction and increase in circulating Factor IX activity in patients with hemophilia B.(1)

The key trial ICER used for evaluation of etranacogene dezaparvovec was the Phase 3 HOPE-B trial. In addition, results from a Phase 2b trial with 3 patients was used in the assessment. Both studies are single-arm trial that included males with moderately severer to severe hemophilia B. The annualized bleeding rate at 52 weeks was assessed as a primary outcome in the HOPE-B while Factor IX activity was considered as a primary outcome for the Phase 2b trial.(12)

The inclusion criteria for the HOPE-B trial included:(13)

- Male
- Age greater than or equal to 18 years of age
- Diagnosis of congenital hemophilia B, classified as severe or moderately severe, and currently on Factor IX prophylaxis
- Greater than 150 previous exposure days of treatment for Factor IX protein

The exclusion criteria for the HOPE-B trial included:(13)

- History of Factor IX inhibitors
- Positive Factor IX inhibitor test at screening
- Positive human immunodeficiency virus (HIV) test at screening , not controlled with anti-viral therapy
- Active infection with hepatitis B or C virus at screening
- History of hepatitis B or C exposure, currently controlled by antiviral therapy at the end of the lead-in phase
- Previous gene therapy treatment
- Receipt of an experimental agent within 60 days prior to screening
- Current participation or anticipated participation within one year after study drug administration in this trial in any other interventional clinical trial involving drugs or devices

The efficacy of Hemgenix was evaluated in a prospective, open-label, single-dose, single-arm, multi-national study in 54 patients. The subjects prospectively completed a lead-in period of at least six months with the intent to receive standard of care routine Factor IX prophylaxis. The subjects then received the indicated single intravenous dose of Hemgenix. and followed up monthly until Month 12, then at 6-month intervals until Year 5.(1)

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allowed to continue prophylaxis during Months 0 to 6. The estimated mean ABR during Months 7 to 18 after Hemgenix treatment was 1.9 bleeds/year with a 95% confidence interval (CI) of (1.0, 3.4), compared with an estimated ABR of 4.1 (95% CI: 3.2, 5.4) during the lead-in period. The ABR ratio (Months 7 to 18 post-treatment/lead-in) was 0.46 (95% CI: 0.26, 0.81), demonstrating non-inferiority or ABR during Month 7 to 18 compared to the lead-in period.(1)

**Safety**

Hemgenix has no FDA labeled contraindications.

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Use this feature to find out if a procedure and diagnosis code pair will be approved, denied or held for review. Simply put in the procedure code, then the diagnosis code, then click "Add Code Pair". If the codes are listed in this policy, we will help you by showing a dropdown to help you.

### Procedure

Please type a procedure code

Enter at least the first 3 characters of the code

### Diagnosis

Please type a diagnosis code

Enter at least the first 3 characters of the code

Add

## CODES

+ **HCPCS**

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## REVISIONS

**01-02-2025**
Added new code for 01/01/2025 J1414

**09-12-2024**
Added new code for 10/1/2024: C9172

**12-01-2023**
Policy reviewed at Medical Policy Committee meeting on 11/8/2023 – no changes to policy.

**03-30-2023**
Added new HCPCS code for 04/01/2023: J1411