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# Etranacogene dezaparvovec-drlb

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## Related Coverage Resources

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## Overview

This policy supports medical necessity review for the gene therapy product, ertanacogene dezaparvovec-drlb (Hemgenix®).

Gene Therapy coverage varies across plans. Refer to the customer's benefit plan document for coverage details.

## Medical Necessity Criteria

**Ertanacogene dezaparvovec-drlb (Hemgenix®) is considered medically necessary for the treatment of Hemophilia B when the individual meets ALL of the following criteria:**

1. Male, 18 years of age or older
2. Documentation of moderately severe or severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level of less than or equal to 2% of normal
3. **ONE** of the following:

a. **BOTH** of the following:
    i. Documentation of receiving routine prophylaxis with Factor IX therapy continuously for at least 2 months
    ii. According to the prescriber, has at least a 150 exposure day history of Factor IX therapy
b. **BOTH** of the following:
    i. History of life-threatening hemorrhage
    ii. On-demand use of Factor IX therapy was required for this life-threatening hemorrhage
c. **BOTH** of the following:
    i. History of repeated, serious spontaneous bleeding episodes
    ii. On-demand use of Factor IX therapy was required for these serious spontaneous bleeding episodes

4. Documentation of **ALL** of the following:
    a. **BOTH** of the following:
        i. Factor IX inhibitor titer testing performed within 30 days before receiving Hemgenix
        ii. No current, or history of, Factor IX inhibitors
    b. Adequate hepatic function as evidenced by **ALL** of the following:
        i. Alanine aminotransferase is less or equal to 2 times the upper limit of normal
        ii. Aspartate aminotransferase is less or equal to 2 times the upper limit of normal
        iii. Total bilirubin levels are less or equal to 2 times the upper limit of normal
        iv. Alkaline phosphatase levels are less or equal to 2 times the upper limit of normal
        v. No evidence of advanced liver impairment and/or advanced fibrosis

            For example, liver elastrography (e.g., greater than or equal to 9 kPA) suggestive of or equal to METAVIR Stage 3 disease.

    c. Adequate renal function as evidenced by **BOTH** of the following:
        i. Estimated creatinine clearance of at least 30 mL/min
        ii. Creatinine levels are less or equal to 2 times the upper limit of normal
    d. Platelet count of at least 50 x $10^9$/L performed within the last 30 days
    e. Prior to receiving Hemgenix, **BOTH** of the following:
        i. Screening for hepatitis B and C is negative
        ii. Is not currently receiving antiviral therapy for a prior hepatitis B virus or C virus exposure
    f. If positive for human immunodeficiency virus, is controlled on antiviral therapy as evidence by adequate CD4+ counts of at least 200/µL or by a viral load of less than or equal 200 copies/mL
5. Prescriber attestation of no other coagulation disorders, besides hemophilia B
6. No prior history of receiving gene therapy
7. Prescriber attestation that prophylactic therapy with Factor IX will not be given once adequate Factor IX levels have been achieved

    Use of episodic Factor IX therapy is acceptable for the treatment of bleeds and for surgery/procedures if needed as determined by the hemophilia specialist physician.

8. Prescriber attestation that, following Hemgenix infusion, **ALL** of the following will be performed:
    a. Liver enzyme testing to monitor for liver enzyme elevations will be done at least weekly for the first 3 months and periodically thereafter
    b. Implementing a course of corticosteroids will be considered if clinically relevant increases in alanine aminotransferase levels
    c. Will undergo monitoring for Factor IX activity at least weekly for the first 3 months and periodically thereafter
    d. If has preexisting risk factors for hepatocellular carcinoma, will receive abdominal ultrasound screenings and be monitored at least annually with alpha fetoprotein elevations in the 5 years following receipt of Hemgenix

        Risk factors include a patient with prior history of hepatitis B and/or C, non-alcoholic fatty liver disease, chronic alcohol consumption, non-alcoholic steatohepatitis, and advanced age.

9. Medication is prescribed by a physician who specializes in hemophilia

**Dosing for Hemophilia B**. The recommended dose of Hemgenix is a single dose, given by intravenous infusion, containing 2 x $10^{13}$ genome copies based on current (within the past 30 days) weight in kilograms. Configuration of the dose-kit is located in the Appendix.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

## Authorization Duration

Authorization is for a one-time approval.

## Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

## Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

| HCPCS Codes | Description |
|---|---|
| J1411 | Injection, etranacogene dezaparvovec-drlb, per therapeutic dose (Code effective 04/01/2023) |

## Background

**OVERVIEW**
Hemgenix, an adeno-associated virus vector-based gene therapy, is indicated for the treatment of adults with hemophilia B (congenital Factor IX deficiency) who: 1) currently use Factor IX prophylaxis therapy; or 2) have current or historical life-threatening hemorrhage; or 3) have repeated, serious spontaneous bleeding episodes.[1]

**Disease Overview**
Hemophilia B is a genetic bleeding disorder caused by missing or insufficient levels of blood Factor IX, a protein required to produce blood clots to halt bleeding.[2-5] The condition is a rare X-linked bleeding disorder that mainly impacts males. Hemophilia B is four times less common than hemophilia A, which is caused by a relative lack of blood Factor VIII. Approximately 30,000 individuals are living with hemophilia in the US and hemophilia B accounts for around 15% to 20% of hemophilia cases, or around 6,000 patients. Symptoms patients may experience include heavy or prolonged bleeding following an injury or after a medical procedure. Bleeding can also occur internally into joints, muscles or internal organs. Spontaneous bleeding events (for example, within the musculoskeletal system and predominantly intra-articular bleeding into the large synovial joints, i.e., the ankles, knees, and elbows, and frequently into the shoulder, wrist, and hip joints) may also occur. Some bleeding events could be life-threatening, for example central nervous system or gastrointestinal hemorrhage.[13] Hemophilia B may be diagnosed when bleeding occurs in infancy or later in life for those with milder disease. There is a strong correlation between Factor IX levels and phenotypic expression of bleeding. Normal plasma levels of Factor IX range from 50% to 150%. The disease is classified based on reduced levels. Mild, moderate, and severe hemophilia B are characterized by Factor IX levels ranging from 6% up to 49%, 1% up to 5%, and < 1%, respectively. Besides Hemgenix, Factor IX products, both recombinant and plasma-derived, are used routinely to prevent bleeding or are given on demand to treat bleeding episodes associated with hemophilia B.

**Clinical Efficacy**
The efficacy of Hemgenix was evaluated in a prospective, open-label, single-dose, single-arm, multinational pivotal study called HOPE-B that involved 54 adult male patients with moderately severe or severe hemophilia B (Factor IX levels ≤ 2%).[1,6-9] Patients prospectively completed a lead-in period of at least 6 months in which standard care routine (defined as the intent of treating with predetermined frequency of infusions [e.g., twice weekly, once every two weeks] as documented in medical records) Factor IX prophylaxis therapy was given.[1, 6-9] This was followed by a single intravenous dose of 2 x $10^{13}$ genome copies/kg of body weight of Hemgenix. Patients were permitted to continue Factor IX prophylaxis during Months 0 to 6 after dosing, if needed, until Factor IX levels were adequate. The estimated mean annualized bleeding rate during Months 7 to 18 following Hemgenix treatment was 1.9 bleeds/year compared with 4.1 bleeds/year during the lead-in period (before Hemgenix administration).[1,6-9] The HOPE-B trial is ongoing.[1] Other data are also available.[10-12]

**Safety**
Monitor patients during administration of Hemgenix and for at least 3 hours after the end of the infusion for infusion reactions. Closely monitor transaminase levels at least once per week for 3 months after Hemgenix administration to assess for the risk of potential hepatotoxicity. Consider corticosteroid treatment if elevations occur. Monitor Factor IX activity and for Factor IX inhibitors.

## References


1. Hemgenix® intravenous infusion [prescribing information]. King of Prussia, PA; Kankakee, IL; and Lexington, MA: CSL Behring and uniQure; November 2022.
2. National Hemophilia Foundation. Hemophilia B. An overview of symptoms, genetics, and treatments to help you understand hemophilia B. Available at: https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b. Accessed on January 11, 2023.
3. Sidonio RF, Malec L. Hemophilia (Factor IX deficiency). *Hematol Oncol Clin N Am*. 2021;35:1143-1155.
4. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting factor concentrates to gene editing. *Lancet*. 2021;397:630-640.
5. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin N Am*. 2022;36:797-812.
6. Hemgenix™ Dossier. CSL Behring. December 2022.
7. Pipe S, Leebeek FWG, Recht M, et al (poster 2139). Durability of bleeding protection and factor IX activity levels are demonstrated in individuals with and without adeno-associated virus serotype 5 neutralizing antibodies (titers < 1:700) with comparable safety in the Phase 3 HOPE-B clinical trial of etranacogene dezaparvovec gene therapy for hemophilia B. Presented at: the American Society of Hematology (ASH) 64th Annual Meeting and Exposition; New Orleans, LA; December 10-13, 2022. Available at: https://ash.confex.com/ash/2022/webprogram/Paper166745.html. Accessed on December 31, 2022.
8. Pipe S, Leebeek FWG, Recht M, et al (poster 2141). Adults with severe or moderately severe hemophilia B receiving etranacogene dezaparvovec in the HOPE-B Phase 3 clinical trial continue to experience a stable increase in mean factor IX activity levels and durable hemostatic protection after 24 months' follow-up. Presented at: the American Society of Hematology (ASH) 64th Annual Meeting and Exposition; New Orleans, LA; December 10-13, 2022. Available at: https://ash.confex.com/ash/2022/webprogram/Paper166135.html. Accessed on December 31, 2022.
9. Miesbach WA, Recht M, Key NS, et al. Durability of Factor IX activity and bleeding rate in people with severe or moderately severe hemophilia B after 5 years of follow-up in the Phase 1/2 study of AMT-060, and after 3 years of follow-up in the Phase 2b and 2 years of follow-up in the Phase 3 studies of etranacogene dezaparvovec (AMT-061). Presented at: the American Society of Hematology (ASH) 64th Annual Meeting and Exposition; New Orleans, LA; December 10-13, 2022. Available at: https://ash.confex.com/ash/2022/webprogram/Paper166810.html. Accessed on December 31, 2022.
10. Von Drygalski A, Giermasz A, Castaman G, et al. Etranacogene dezaparvovec (AMT-061 phase 2b); normal/near normal FIX activity and bleed cessation in hemophilia B. *Blood*. 2019;3(21):3241-3247.

11. Von Drygalski A, Gomez E, Giermasz A, et al. Stable and durable factor IX levels in hemophilia B patients over 3 years post etranacogene dezaparvovec gene therapy. *Blood Adv*. 2022 Dec 9. [Online ahead of print].
12. Shah J, Kim H, Sivamurthy K, et al. Comprehensive analysis and prediction of long-term durability of factor IX activity following etranacogene dezaparvovec gene therapy in the treatment of hemophilia B. *Curr Med Res Opin*. 2022 Oct 25. [Online ahead of print].

## Supplemental References

13. World Federation of Hemophilia Guidelines for the Management of Hemophilia. Available at: https://www1.wfh.org/publications/files/pdf-1863.pdf. Accessed on December 13, 2022.

**APPENDIX**

Hemgenix Multi-Vial Kits.[1]

| Total Number of Vials per Kit | Patient Body Weight | Total Volume per Kit | NDC Number |
|---|---|---|---|
| 10 | 46 to 50 kg | 100 | 0053-0100-10 |
| 11 | 51 to 55 kg | 110 | 0053-0110-11 |
| 12 | 56 to 60 kg | 120 | 0053-0120-12 |
| 13 | 61 to 65 kg | 130 | 0053-0130-13 |
| 14 | 66 to 70 kg | 140 | 0053-0140-14 |
| 15 | 71 to 75 kg | 150 | 0053-0150-15 |
| 16 | 76 to 80 kg | 160 | 0053-0160-16 |
| 17 | 81 to 85 kg | 170 | 0053-0170-17 |
| 18 | 86 to 90 kg | 180 | 0053-0180-18 |
| 19 | 91 to 95 kg | 190 | 0053-0190-19 |
| 20 | 96 to 100 kg | 200 | 0053-0200-20 |
| 21 | 101 to 105 kg | 210 | 0053-0210-21 |
| 22 | 106 to 110 kg | 220 | 0053-0220-22 |
| 23 | 111 to 115 kg | 230 | 0053-0230-23 |
| 24 | 116 to 120 kg | 240 | 0053-0240-24 |
| 25 | 121 to 125 kg | 250 | 0053-0250-25 |
| 26 | 126 to 130 kg | 260 | 0053-0260-26 |
| 27 | 131 to 135 kg | 270 | 0053-0270-27 |
| 28 | 136 to 140 kg | 280 | 0053-0280-28 |
| 29 | 141 to 145 kg | 290 | 0053-0290-29 |
| 30 | 146 to 150 kg | 300 | 0053-0300-30 |
| 31 | 151 to 155 kg | 310 | 0053-0310-31 |
| 32 | 156 to 160 kg | 320 | 0053-0320-32 |
| 33 | 161 to 165 kg | 330 | 0053-0330-33 |
| 34 | 166 to 170 kg | 340 | 0053-0340-34 |
| 35 | 171 to 175 kg | 350 | 0053-0350-35 |
| 36 | 176 to 180 kg | 360 | 0053-0360-36 |
| 37 | 181 to 185 kg | 370 | 0053-0370-37 |
| 38 | 186 to 190 kg | 380 | 0053-0380-38 |
| 39 | 191 to 195 kg | 390 | 0053-0390-39 |
| 40 | 196 to 200 kg | 400 | 0053-0400-40 |
| 41 | 201 to 205 kg | 410 | 0053-0410-41 |
| 42 | 206 to 210 kg | 420 | 0053-0420-42 |
| 43 | 211 to 215 kg | 430 | 0053-0430-43 |
| 44 | 216 to 220 kg | 440 | 0053-0440-44 |
| 45 | 221 to 225 kg | 450 | 0053-0450-45 |
| 46 | 226 to 230 kg | 460 | 0053-0460-46 |
| 47 | 231 to 235 kg | 470 | 0053-0470-47 |
| 48 | 236 to 240 kg | 480 | 0053-0480-48 |

NDC – National Drug Code.