

Hemgenix® (etranacogene dezaparvovec-drlb intravenous infusion)

When requesting Hemgenix® (etranacogene dezaparvovec-drlb intravenous infusion), the individual requiring treatment must be diagnosed with the following FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved indication

Hemgenix is indicated 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.

Coverage Guidelines

Hemophilia B

The individual must meet all of the following criteria for authorization:

- Is male;
- Is greater than or equal to 18 years of age;
- Has moderately severe or severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level of $\leq 2\%$ of normal;
- Meets one of the following:
 - Meets both of the following:
 - I. Has been receiving routine prophylaxis with Factor IX therapy continuously for at least 2 months; AND
 - II. Has a history of use of Factor IX therapy for at least 150 exposure days; OR
 - Meets both of the following:
 - I. Has a history of life-threatening hemorrhage; AND
 - II. On-demand use of Factor IX therapy was required for this life-threatening hemorrhage; OR
 - Meets both of the following:
 - I. Has a history of repeated, serious spontaneous bleeding episodes; AND
 - II. On-demand use of Factor IX therapy was required for these serious spontaneous bleeding episodes; AND
- Meets all of the following criteria:
 - Factor IX inhibitor titer testing has been performed within 30 days before receipt of Hemgenix; AND
 - Patient does not currently have an inhibitor to Factor IX; AND

- Patient does not have a history of Factor IX inhibitors;
- Prophylactic therapy with Factor IX will not be given after Hemgenix administration once adequate Factor IX levels have been achieved;
Note: 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.
- Has not received Hemgenix in the past;
- Meets both of the following:
 - Does not have active infection with hepatitis B virus or hepatitis C virus; AND
 - Is not currently receiving antiviral therapy for a prior hepatitis B virus or C virus exposure;
- Does not have uncontrolled human immunodeficiency virus;
Note: A patient testing positive for human immunodeficiency virus can still qualify for Hemgenix if controlled on antiviral therapy with CD4+ counts $\geq 200/\mu\text{L}$ or by a viral load of ≤ 200 copies/mL.
- Has undergone liver health assessment within the last 30 days and all of the following levels are ≤ 2 times the upper limit of normal:
 - Alanine aminotransferase; AND
 - Aspartate aminotransferase; AND
 - Total bilirubin levels; AND
 - Alkaline phosphatase levels;
- Does not have evidence of advanced liver impairment and/or advanced fibrosis;
Note: For example, liver elastography (e.g., ≥ 9 kPA) suggestive of or equal to METAVIR Stage 3 disease.
- Within the last 30 days, platelet counts were evaluated and were $\geq 50 \times 10^9/\text{L}$;
- Has adequate renal function as defined by meeting both of the following:
 - Has an estimate creatinine clearance ≥ 30 mL/min; AND
 - Creatinine levels are ≤ 2 times the upper limit of normal;
- Does not have another coagulation disorder, besides hemophilia B;
- After Hemgenix infusion, the following will be performed:
 - Both of the following will be done:
 - I. Liver enzyme testing to monitor for liver enzyme elevations will be done at least weekly for the first 3 months and periodically thereafter; AND
 - II. A course of corticosteroids will be considered if the patient experiences clinically relevant increases in alanine aminotransferase levels; AND
 - Individual will undergo monitoring for Factor IX activity at least weekly for the first 3 months and periodically thereafter; AND
 - Individuals with preexisting risk factors for hepatocellular carcinoma will receive abdominal ultrasound screenings and be monitored at least annually with alpha fetoprotein levels in the 5 years following receipt of Hemgenix;
Note: 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.
- Hemgenix is prescribed by a physician who specializes in hemophilia.

Approval duration: one time (per lifetime)

Recommended Dosing

The recommended dose of Hemgenix is 2×10^{13} genome copies per kilogram of body weight administered as an intravenous infusion.

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].