Hemgenix (etranacogene dezaparvovec)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Hemophilia B is a type of bleeding disorder caused by low levels of clotting factor IX (factor IX deficiency), preventing blood from clotting properly. Because factor IX genes are on the X chromosome, severe hemophilia is most common in males because males have only one X chromosome. While females can also get hemophilia, it is usually milder. The severity of hemophilia B is classified based on clotting factor activity level detected in blood and bleeding severity:

- Mild disease:
    - Clotting factor activity level more than 5% but less than 40% of normal (more than 5 but less than 40 units/dL)
    - Frequency of bleeding episodes varies from once a year to once a decade (usually after major trauma)
- Moderate disease:
    - Clotting factor activity level 1% to 5% of normal (1-5 units/dL)
    - Frequency of bleeding episodes varies from one per month to one per year (usually after trauma or minor injury)

- Severe disease:
    - Clotting factor activity level less than 1% of normal (less than 1 unit/dL)
    - Frequent spontaneous bleeding episodes (e.g., 2-5 per month) and after minor injury

Treatment depends on how severe the condition is, and usually involves replacing the missing clotting factor through factor replacement therapy. Factor replacement therapy is given mainly to prevent bleeding or to treat a bleed when it happens. Hemgenix (etranacogene dezaparvovec) is an adeno-associated virus vector-based gene therapy 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.

Definitions

"**Congenital**" means a condition present from birth.

"**Endogenous**" refers to factors made inside the body.

"**Hemophilia**" is a condition in which blood doesn't clot normally due to missing a protein. There are two main types, hemophilia A (factor VIII is missing or very low) or hemophilia B (factor IX is missing or very low).

"**Hemorrhage**" is the medical term for bleeding.

"**Prophylaxis**" is to prevent a disease from occurring.

"**Spontaneous**" is to happen without cause or involuntarily.

Medical Necessity Criteria for Authorization

The Plan considers **Hemgenix (etranacogene dezaparvovec)** medically necessary when **ALL** of the following criteria are met:

1. Prescribed by or in consultation with a hematologist***; AND***
2. The member meets **ALL** of the following:
    a. is a male 18 years of age or older***; and***

b. has a diagnosis of congenital hemophilia B and documentation of at least **ONE** of the following:
    i. Known severe or moderately severe factor IX deficiency (defined as less than or equal to (≤) 2% of normal circulating endogenous factor IX)***; or***
    ii. Is on continuous routine factor IX prophylaxis***; or***
    iii. Have current or historical life-threatening hemorrhage***; or***
    iv. Have repeated, serious spontaneous bleeding episodes***; AND***

3. The member does **NOT** have ANY of the following:
    a. Advanced hepatic impairment, including cirrhosis or advanced liver fibrosis (suggestive of or equal to METAVIR Stage 3 disease; e.g., a FibroScan score of ≥9 kPa is considered equivalent)***; or***
    b. History of factor IX inhibitors or positive test result for human factor IX inhibitors***; or***
    c. Human Immunodeficiency Virus (HIV) not controlled with anti-viral therapy (as shown by CD4+ counts ≤200/µL)***; or***
    d. Prior treatment with gene therapy***; or***
    e. Uncontrolled Hepatitis B or C.

Experimental or Investigational / Not Medically Necessary

Hemgenix (etranacogene dezaparvovec) for any other indication is *not covered* by the Plan, as it is considered experimental or investigational. Non-covered indications include, but are not limited to, the following:

- Use in individuals whose sex is not male, unless the prescriber is able to provide information that the requested agent is medically appropriate for the patient's sex.
- Use in males less than 18 years of age. The safety and efficacy of Hemgenix (etranacogene dezaparvovec) in pediatric patients have not been established.
- Re-treatment [Hemgenix (etranacogene dezaparvovec) is indicated for one-time single-dose intravenous use only].

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*

96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
J1411	Injection, etranacogene dezaparvovec-drlb, per therapeutic dose
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
D67	Hereditary factor IX deficiency

References

1. Alshaikhli A, Rokkam VR. Hemophilia B. Updated February 8, 2022. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560792/. Accessed September 21, 2022.
2. Buckner TW, Bocharova I, Hagan K, et al. Health care resource utilization and cost burden of hemophilia B in the United States. Blood Adv. 2021;5(7):1954-1962. doi:10.1182/bloodadvances.2020003424
3. Carcao M et al: Hemophilia A and B. In: Hoffman R et al, eds: Hematology: Basic Principles and Practice. 7th ed. Philadelphia, PA: Elsevier; 2018:2001-22
4. Hemgenix (etranacogene dezaparvovec) [prescribing information]. Kankakee, IL: CSL Behring LLC; November 2022.
5. Miesbach W, Meijer K, Coppens M, et al. Gene therapy with adeno-associated virus vector 5-human factor IX in adults with hemophilia B. Blood. 2018;131(9):1022-1031. doi:10.1182/blood-2017-09-804419
6. Miller CH. The clinical genetics of hemophilia B (factor IX deficiency). Appl Clin Genet. 2021;14:445-454. doi:10.2147/TACG.S288256
7. National Hemophilia Foundation: Guidelines for Emergency Department Management of Individuals With Hemophilia and Other Bleeding Disorders. NHF website. Published September 17, 2017. Accessed November 2022. https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/Guidelines-for-Emergency-Department-Management-of-Individuals-with-Hemophilia-and-Other-Bleeding-Disorders
8. National Hemophilia Foundation: MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. NHF website. Published April 23,

2018. Accessed November 2022. https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Concerning-Products-Licensed-for-the-Treatment-of-Hemophilia-and-Other-Bleeding-Disorders

9. Perrin GQ, Herzog RW, Markusic DM. Update on clinical gene therapy for hemophilia. Blood. 2019;133(5):407-414. doi:10.1182/blood-2018-07-820720
10. Pipe SW, Leebeek FWG, Recht M, et al. Gene therapy with etranacogene dezaparvovec for hemophilia B. N Engl J Med. 2023;388(8):706-718. doi:10.1056/NEJMoa2211644[PubMed 36812434]
11. Samelson-Jones BJ, Finn JD, George LA, Camire RM, Arruda VR. Hyperactivity of factor IX Padua (R338L) depends on factor VIIIa cofactor activity. JCI Insight. 2019;5(14):e128683. doi:10.1172/jci.insight.128683
12. Samelson-Jones BJ, Finn JD, Raffini LJ, et al. Evolutionary insights into coagulation factor IX Padua and other high-specific-activity variants. Blood Adv. 2021;5(5):1324-1332. doi:10.1182/bloodadvances.2019000405
13. Soucie JM, Miller CH, Dupervil B, Le B, Buckner TW. Occurrence rates of haemophilia among males in the United States based on surveillance conducted in specialized haemophilia treatment centres. Haemophilia. 2020;26(3):487-493. doi:10.1111/hae.13998
14. Spronck EA, Liu YP, Lubelski J, et al. Enhanced factor IX activity following administration of AAV5-R338L "Padua" factor IX versus AAV5 WT human factor IX in NHPs. Mol Ther Methods Clin Dev. 2019;15:221-231. doi:10.1016/j.omtm.2019.09.005
15. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia panelists and co-authors. WFH Guidelines for the Management of Hemophilia, 3rd edition [published correction appears in Haemophilia. July 2021;27(4):699]. Haemophilia. 2020;26 Suppl 6:1-158. doi:10.1111/hae.14046
16. 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 [published correction appears in Blood Adv. August 11, 2020;4(15):3668]. Blood Adv. 2019 Nov 12;3(21):3241-3247. doi:10.1182/bloodadvances.2019000811

Clinical Guideline Revision / History Information

Original Date: 12/08/2022
Reviewed/Revised: 06/01/2023, 12/14/2023