PRIOR AUTHORIZATION POLICY

POLICY: Hemophilia – Gene Therapy – Hemgenix Prior Authorization Policy
- Hemgenix® (etranacogene dezaparvovec-drlb intravenous infusion – CSL Behring and uniQure)

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OVERVIEW

Hemgenix, an adeno-associated virus (AAV) 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.[1,2] The recommended dose of Hemgenix is 2 x 10^{13} genome copies per kg of body weight given as a one-time (per lifetime) single dose as an intravenous infusion.

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.[3-6] 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 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 may also occur. Complications in patients with hemophilia B include joint disease and hemarthrosis. 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 is characterized by Factor IX levels ranging from 6% up to 49%, 1% up to 5%, and < 1%, respectively. Besides gene therapies for the treatment of hemophilia B, 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 males with moderately severe or severe hemophilia B (Factor IX levels ≤ 2%).[1] Patients prospectively completed a lead-in period of at least 6 months in which standard care routine Factor IX prophylaxis therapy was given. This was followed by a single intravenous dose 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. Prior to screening, patients had been on stable prophylactic therapy for at least 2 months and had greater than 150 exposure days of treatment with a Factor IX product.[2] Factor IX inhibitors (or a history), uncontrolled human immunodeficiency virus (HIV) infection, or advanced liver fibrosis prevented participation. Adequate hepatic and renal function were required. 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] At 18 months after treatment, Factor IX activity had increased by 34.3%. The HOPE-B trial is ongoing.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Hemgenix. Approval is recommended for those who meet the Criteria for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Hemgenix as well as the monitoring required for adverse events and long-term efficacy, approval requires Hemgenix to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one-time (per lifetime) as a single dose. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. In the criteria for Hemgenix, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: males are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression. All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required for use of Hemgenix as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Hemgenix is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Hemophilia B.** Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, and P):
   - **A)** Patient is male*; AND
   - **B)** Patient is ≥ 18 years of age; AND
   - **C)** Patient has not received a gene therapy for hemophilia B in the past **[verification in claims history required]**; AND
     Note: If no claim for Hemgenix or Beqvez (fidanacogene elaparvovec intravenous infusion) is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Hemgenix or Beqvez.
   - **D)** Patient has moderately severe or severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level ≤ 2% of normal **[documentation required]**; AND
   - **E)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** According to the prescribing physician, the patient has a history of use of Factor IX therapy for ≥ 150 exposure days; OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has a history of life-threatening hemorrhage; AND
       - **b)** On-demand use of Factor IX therapy was required for this life-threatening hemorrhage; OR
     - **iii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has a history of repeated, serious spontaneous bleeding episodes; AND
       - **b)** On-demand use of Factor IX therapy was required for these serious spontaneous bleeding episodes; AND
   - **F)** Patient meets ALL of the following (i, ii, and iii):
     - **i.** Factor IX inhibitor titer testing has been performed within 30 days **[documentation required]**; AND

ii. Patient is negative for Factor IX inhibitors **[documentation required]**; AND
iii. Patient does not have a of Factor IX inhibitors **[documentation required]**; AND

G) Prophylactic therapy with Factor IX will not be given after Hemgenix administration once adequate Factor IX levels have been achieved; AND
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 physician.

H) Patient meets BOTH of the following (i and ii):
i. Patient does not have an active infection with hepatitis B virus or hepatitis C virus **[documentation required]**; AND
ii. Patient is not currently receiving antiviral therapy for a prior hepatitis B virus or hepatitis C virus exposure **[documentation required]**; AND

I) According to the prescribing physician, the patient does not have uncontrolled human immunodeficiency virus infection; AND

J) Patient has undergone liver function testing within 30 days and meets ALL of the following (i, ii, iii, and iv):
i. Alanine aminotransferase level is ≤ two times the upper limit of normal **[documentation required]**; AND
ii. Aspartate aminotransferase level is ≤ two times the upper limit of normal **[documentation required]**; AND
iii. Total bilirubin level is ≤ two times the upper limit of normal **[documentation required]**; AND
iv. Alkaline phosphatase level is ≤ two times the upper limit of normal **[documentation required]**; AND

K) Patient does not have evidence of advanced liver impairment and/or advanced fibrosis; AND
Note: For example, liver elastography (e.g., ≥ 9 kPA) suggestive of or equal to METAVIR Stage 3 disease.

L) Within 30 days, the platelet count was ≥ 50 x 10^9/L **[documentation required]**; AND

M) Within 30 days, patient meets ONE of the following (i or ii):
i. Patient has an estimated creatinine clearance ≥ 30 mL/min **[documentation required]**; OR
ii. Creatinine level is ≤ two times the upper limit of normal **[documentation required]**; AND

N) The medication is prescribed by a hemophilia specialist physician; AND

O) Current patient body weight has been obtained within 30 days **[documentation required]**; AND

P) If criteria A through O are met, approve one dose (kit) of Hemgenix to provide for a one-time (per lifetime) single dose of 2 x 10^{13} genome copies per kg of body weight by intravenous infusion **[verification required]**. Table 1 provides the kit size and the National Drug Codes (NDCs).

***** Refer to the Policy Statement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Hemgenix is not recommended in the following situations:

1. **Prior Receipt of Gene Therapy**. Prior receipt of gene therapy was a reason for patient exclusion in the pivotal study.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Table 1. Hemgenix Multi-Vial Kits.[1]
NDC – National Drug Code.

REFERENCES

1. Hemgenix® intravenous infusion [prescribing information]. King of Prussia, PA; Kankakee, IL; and Lexington, MA: CSL Behring and uniQure; November 2022.
2. Pipe SW, Leebeek FWG, Recht M, et al. Gene therapy with etranacogene dexaparvovec for hemophilia B. *N Engl J Med*. 2023;388:706-718.
3. National Bleeding Disorders 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 May 3, 2024.
4. Sidonio RF, Malec L. Hemophilia (Factor IX deficiency). *Hematol Oncol Clin N Am*. 2021;35:1143-1155.
5. 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.
6. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin N Am*. 2022;36:797-812.