POLICY: Hemophilia – Gene Therapy – Hemgenix Utilization Management Medical Policy

- Hemgenix® (etranacogene dezaparvovec-drlb intravenous infusion – CSL Behring and uniQure)

EFFECTIVE DATE: 5/15/2023
LAST REVISION DATE: 03/01/2023

COVERAGE CRITERIA FOR: All UCare Plans

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 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 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 Factor IX prophylaxis therapy was given.[1] This was followed by a single intravenous dose of 2×10^{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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Hemgenix. 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 or in consultation with a physician who specializes in the condition being treated. For certain criteria, verification is required as noted by **[verification required by prescriber]**. All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation. In the approval indication for Hemgenix, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: men 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. Some clients have elected Embarc Benefit Protection. For these clients, the Medical Director will coordinate with eviCore to ensure the Embarc Benefit Protection portion of the review has been completed. If the Embarc Benefit Protection portion of the review has not been completed, the Medical Director will route to Embarc@eviCore.com prior to completing the review.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, 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 dose if the patient meets the following criteria (A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P, and Q):
   - **A)** Patient is male*; AND
   - **B)** Patient is greater than or equal to 18 years of age; AND
   - **C)** Patient has moderately severe or severe hemophilia B as evidence by a baseline (without Factor IX replacement therapy) Factor IX level of ≤ 2% of normal **[documentation required]**; AND
   - **D)** Patient meets one of the following (i, ii, or iii):
     - **i.** Patient meets both of the following (a and b):
       - **a)** Patient has been receiving routine prophylaxis with Factor IX therapy continuously for at least 2 months **[documentation required]**; AND
       - **b)** According to the prescribing physician, the patient has a history of use of Factor IX therapy for at least 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

E) Patient meets all of the following criteria (i, ii, and iii):
- **i.** Factor IX inhibitor titer testing has been performed within 30 days before receipt of Hemgenix **[documentation required]**; AND
- **ii.** Patient does not currently have an inhibitor to Factor IX **[documentation required]**; AND
- **iii.** Patient does not have a history of Factor IX inhibitors **[documentation required]**; AND

F) Prescriber attests that 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.

G) Patient has not received Hemgenix in the past **[verification required by prescriber]**; AND
Note: Verify through claims history that the patient has not previously received Hemgenix AND, if no claim for Hemgenix is present, the prescriber must attest that the patient has not previously received Hemgenix.

H) Patient must meet 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 C virus exposure **[documentation required]**; AND

I) Patient does not have uncontrolled human immunodeficiency virus **[documentation required]**; AND
Note: A patient testing positive for human immunodeficiency virus can still qualify for Hemgenix if controlled on antiviral therapy with CD4+ counts ≥ 200/µL or by a viral load of ≤ 200 copies/mL.

J) Patient has undergone a liver health assessment within the last 30 days and meets all of the following (i, ii, iii, and iv):
- **i.** Alanine aminotransferase is ≤ 2 times the upper limit of normal **[documentation required]**; AND
- **ii.** Aspartate aminotransferase is ≤ 2 times the upper limit of normal **[documentation required]**; AND
- **iii.** Total bilirubin levels are ≤ 2 times the upper limit of normal **[documentation required]**; AND
- **iv.** Alkaline phosphatase levels are ≤ 2 times the upper limit of normal **[documentation required]**; AND

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

L) Within the last 30 days, platelet counts were evaluated and were ≥ 50 x 10^9/L **[documentation required]**; AND

M) Patient has adequate renal function as defined by meeting both of the following (i and ii):
- **i.** Patient has an estimated creatinine clearance ≥ 30 mL/min **[documentation required]**; AND
- **ii.** Creatinine levels are ≤ 2 times the upper limit of normal **[documentation required]**; AND

N) Physician attests that the patient does not have another coagulation disorder, besides hemophilia B; AND

O) Following Hemgenix infusion, the physician attests that the following will be performed (i, ii, and iii):
- **i.** Patient meets both of the following (a and b):
  - **a)** Liver enzyme testing to monitor for liver enzyme elevations will be done at least weekly for the first 3 months and periodically thereafter; AND

b) Implementing a course of corticosteroids will be considered if the patient experiences clinically relevant increases in alanine aminotransferase levels; AND

ii. Patient will undergo monitoring for Factor IX activity at least weekly for the first 3 months and periodically thereafter; AND

iii. Patients with preexisting risk factors for hepatocellular carcinoma will receive abdominal ultrasound screenings and be monitored at least annually for alpha fetoprotein elevations in the 5 years following receipt of Hemgenix; AND
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.

P) Medication is prescribed by a physician who specializes in hemophilia; AND

Q) If criteria A through P are met, approve one dose (kit) of Hemgenix to provide for a one time (per lifetime) dose of 2 x 10^{13} genome copies based on current body weight in kg (within the past 30 days) **[documentation required]** by intravenous infusion. Table 1 provides the kit size and the National Drug Codes (NDCs).

***** Refer to the Policy Statement.

Dosing. The recommended dose of Hemgenix is a single one time (per lifetime) intravenous infusion of 2 x 10^{13} genome copies based on current body weight in kg (within the past 30 days).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Hemgenix is not recommended in the following situations:

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