Jefferson Health Plans | Health Partners Plans

DR.019.A Hemgenix® (Etranacogene dezaparvovec-drlb)

Original Implementation Date : 7/1/2024
Version [A] Date : 7/1/2024
Last Reviewed Date: 6/19/2024

PRODUCT VARIATIONS

This policy applies to Medicaid, CHIP and Medicare product lines.

Gene therapy is a benefit exclusion for Individual and Family (ACA) product lines and therefore, non-covered.

POLICY STATEMENT

We consider Hemgenix® (Etranacogene dezaparvovec-drlb) medically necessary for its FDA approved indications when the prior authorization listed in this policy are met.

FDA INDICATIONS

Gene Therapy is the introduction, removal, or change in the content of a person's genetic code with the goal of treating or curing a disease. It includes therapies such as gene transfer, gene modified cell therapy, and gene editing.

- Hemgenix® 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.

OFF-LABEL USE

N/A

PRIOR AUTHORIZATION CRITERIA

Prior authorization is required for Hemgenix® (Etranacogene dezaparvovec-drlb).

Hemgenix® (Etranacogene dezaparvovec-drlb) may be considered medically necessary when All of the following apply:

1. FDA approved indication.
2. FDA approved age (18 years and older).
3. Must have severe disease defined as a factor IX levels less than 1% of normal OR moderately severe hemophilia B defined as a Factor IX levels ≥ 1% ≤ 2% (greater than or equal to 0.01 IU/mL to less than or equal to 0.02 IU/mL)
4. Must have one of the following:
    a. Documentation of current or historical life-threatening hemorrhage or repeated, serious spontaneous bleeding episodes.
    b. Documentation of treatment with factor IX therapy with greater than 150 prior exposure days to treatment.
5. Prescribed by or in consultation with a hematologist.
6. Documentation of negative Factor IX inhibitor test result within the past 30 days.
7. If positive for Factor IX inhibitor (by history (greater than or equal to 0.6 Bethesda units) a negative test result needed within 2 weeks.
8. Member has not previously received gene therapy treatment.

SAFETY AND MONITORING

Etranacogene dezaparvovec-drlb (Hemgenix®)

Risk factors:

1. **Infusion reactions**: Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or interrupt administration. Re-start administration at a slower infusion once resolved.

2. **Hepatotoxicity:** Closely monitor transaminase levels once per week for 3 months after Hemgenix® administration to mitigate the risk of potential hepatotoxicity. Continue to monitor transaminases in all patients who developed liver enzyme elevations until liver enzymes return to baseline. Consider corticosteroid treatment should elevations occur.

3. **Hepatocellular carcinogenicity:** For patients with preexisting risk factors (e.g., cirrhosis, advanced hepatic fibrosis, hepatitis B or C, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption, non-alcoholic steatohepatitis (NASH), and advanced age), perform regular (e.g., annual) liver ultrasound and alpha-fetoprotein testing following administration.

4. **Vector distribution in blood (within the body), and vector shedding in semen and other excreta and secreta can occur post-infusion**. It is not known how long this will continue. Patients should not donate blood, organs, tissues, or cells for transplantation.

Monitoring:

1. After Hemgenix® administration, regularly monitor patient's Factor IX activity and Factor IX inhibitors.

2. Hemgenix® can elevate certain liver enzymes. Weekly blood tests will be required to monitor for this for 3 months after treatment. Corticosteroid treatment may be necessary if this occurs.

DOSAGE AND ADMINISTRATION

Hemgenix® is a suspension for intravenous infusion. Hemgenix® is provided in kits containing 10 to 48 single-use vials, each kit constituting a dosage unit based on the patient's body weight.

Hemgenix® has a nominal concentration of 1 x 10^{13} gc/mL, and each vial contains an extractable volume of not less than 10 mL.

- **Administration:** Single-use intravenous infusion only.

- **Dose:** The recommended dose is 2 x 10^{13} genome copies (gc) per kilogram (kg) of body weight (or 2 mL/kg body weight) administered as an intravenous infusion after dilution with 0.9% sodium chloride solution (normal saline) at a constant infusion rate of 500mL/hour (8mL/min).

BENEFIT APPLICATION

Medical policies do not constitute a description of benefits. This medical necessity policy assists in the administration of the member's benefits which may vary by line of business. Applicable benefit documents govern which services/items are eligible for coverage, subject to benefit limits, or excluded completely from coverage.

This policy is invoked only when the requested service is an eligible benefit as defined in the Member's applicable benefit contract on the date the service was rendered. Services determined by the Plan to be investigational or experimental are excluded from coverage for all lines of business. For Medicaid members under 21 years old, benefits and coverage are always based on medical necessity review.

BACKGROUND

Etranacogene dezaparvovec-drlb (Hemgenix®).

Hemophilia B is a rare genetic bleeding disorder in which affected individuals have insufficient levels of FIX due to a mutation on the F9 gene.

Hemophilia B is classified as mild, moderate, or severe based upon the activity level of factor IX. Individuals with mild hemophilia have factor IX levels between 5 and 40% of normal. Those with moderate hemophilia have factor levels from 1 to 5% of normal.

Patients with severe hemophilia have factor levels less than 1% of normal. Symptoms may vary greatly from one person to another depending on severity. Hemophilia B occurs in approximately 1 in 25,000 male births. Although many hemophilia B carrier females do not have symptoms, an estimated 10-25% will develop mild symptoms and females have also been reported with moderate and severe symptoms. Individuals with severe hemophilia B are usually diagnosed around birth or within the first 1-2 years of life; those with moderate hemophilia B, five to six years of age; and individuals with mild hemophilia B may not be diagnosed until later in life and even into adulthood. Clotting factors are the treatment of choice for people with hemophilia as they are very safe and effective for treating and preventing bleeds.

The World Federation of Hemophilia (WFH) 2020 treatment guidelines do not express a preference for recombinant over plasma-derived clotting factor concentrates and state the choice between these classes of product must be made according to availability, cost, and patient preferences. For patients with a severe phenotype, WFH strongly recommends patients be on prophylaxis sufficient to prevent bleeds at all times, but that prophylaxis should be individualized, taking into consideration patient bleeding phenotype, joint status, individual pharmacokinetics, and patient self-assessment and preference. Recombinant activated factor VIIa, a bypassing agent, is recommended for the treatment and prevention of bleeding complications in patients with hemophilia B who develop FIX inhibitors.

Hemgenix® (etranacogene dezaparvovec-drlb) is an adeno-associated viral vector-based gene therapy for intravenous infusion after dilution. Hemgenix® is a non-replicating recombinant AAV5 containing a codon-optimized DNA sequence of the gain-of-function Padua variant of human Factor IX (variant R338L), under control of a liver-specific promotor 1 (LP1).

Single intravenous infusion of H results in cell transduction and increase in circulating Factor IX activity in patients with Hemophilia B. The mean Factor IX activity levels over time, as measured by one-stage [activated Partial Thromboplastin Time (aPTT)-based] assay. Subjects achieved a mean (± SD) uncontaminated (i.e., excluding measurements within five half-lives of Factor IX replacement therapy) Factor IX activity levels of 39% (± 18.7), 41.5% (± 21.7), 36.9% (± 607 21.4) and 36.7 (± 19.0) of normal, respectively, at 6, 12, 18 and 24 months. The time to onset of Factor IX protein expression post-dose was detectable by first uncontaminated measurement at Week 3 in the clinical efficacy study (N = 54). Hemgenix® is not intended for administration in women. No adverse effects on mating rate and fertility indices or fetal weights were observed in healthy naïve female mice mated with healthy male mice that were intravenously administered a predecessor of Hemgenix® product 6 days prior to mating. Vector DNA was not detected in the

uterus, placenta, or fetus.

CLINICAL EVIDENCE

Etranacogene dezaparvovec-drlb (Hemgenix®)

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. The efficacy of Hemgenix® was evaluated in a prospective, open-label, single-dose, single arm, multi-national study (N = 54). The study enrolled adult male subjects aged 19 to 75 years, with severe or moderately severe Hemophilia B, who received a single intravenous dose of 2 × 1013 gc/kg body weight of Hemgenix® and entered a follow-up period of 5 years. The study is on-going.

The main efficacy outcome was a non-inferiority test of annualized bleeding rate (ABR) during Months 7 to 18 after Hemgenix® treatment compared with ABR during the lead-in period. All bleeding episodes, regardless of investigator assessment, were counted. Subjects were allowed to continue prophylaxis during Months 0 to 6. The estimated mean ABR during Months 7 to 18 after Hemgenix® treatment was 1.9 bleeds/year with a 95% confidence interval (CI) of (1.0, 3.4), compared with an estimated mean ABR of 4.1 [95% CI: 3.2, 5.4] during the lead-in period. The ABR ratio (Months 7 to 18 post-treatment / lead-in) was 0.46 [95% CI: 0.26, 0.81], demonstrating noninferiority of ABR during Months 7 to 18 compared to the lead-in period.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

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HCPCS Code	Description
J1411	Etranacogene dezaparvovec-drlb (Hemgenix®).

ICD-10 Codes	Description
N/A	N/A

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making.

Policy Bulletins are developed by us to assist in administering plan benefits and constitute neither offers of coverage nor medical advice.

This Policy Bulletin may be updated and therefore is subject to change.

For Health Choices (Medicaid) and Children's Health Insurance Program (CHIP) products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
New policy.	A	7/1/2024

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REFERENCES

1. Package insert- *HEMGENIX.* CSL Behring: 2022. Available at: Hemgenix-Prescribing-Information.pdf (cslbehring.com).

2. Package insert- *HEMGENIX®.* U.S. Food and Drug Administration: 2022. Available at: https://www.fda.gov/media/163467/download.

3. Etranacogene Dezaparvovec. Lexi-drugs. Lexicomp. Wolters Kluwer Health, Inc. Updated 1/19/23. https://online-lexi-com.libproxy.temple.edu/lco/action/doc/retrieve/docid/patch_f/7290387?cesid=9Z7486Gwmu3&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dhemgenix%26t%3Dname%26acs%3Dfalse%26acq%3D hemgenix#

4. CSL Behring. FDA accepts CSL Behring's biologics license application for etranacogene dezaparvovec for priority review. 2022 May 24. Available at: https://www.cslbehring.com/newsroom/2022/fda- bla-etranacogenedezaparvovec. Accessed on January 9, 2023.

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