Hemgenix® (Etranacogene Dezaparvovec-Drlb)

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Ü Instructions for Use

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Related Policies
None

Applicable States

This Medical Benefit Drug Policy applies to Individual Exchange benefit plans in all states except for Massachusetts, Nevada, and New York.

Coverage Rationale

Hemophilia B (i.e., Congenital Factor IX Deficiency, Christmas Disease)

Hemgenix is proven and medically necessary for the treatment of Hemophilia B (congenital Factor IX deficiency) when all of the following criteria are met [1,3,10]:

- Patient is 18 years of age or older; **and**
- **One** of the following:
  - **Both** of the following:
    - Diagnosis of severe hemophilia B; **and**
    - Documentation of endogenous Factor IX levels less than 1% of normal Factor IX (< 0.01 IU/mL)

    or
  - **All** of the following:
    - Diagnosis of moderately severe hemophilia B; **and**
    - Documentation of endogenous Factor IX levels ≥ 1% ≤ 2% (greater than or equal to 0.01 IU/mL to less than or equal to 0.02 IU/mL); **and**
    - **One** of the following:
      - Patient has current or historical life-threatening hemorrhage; **or**
      - Patient has repeated, serious spontaneous bleeding episodes

  and
- **One** of the following:
  - Patient currently uses Factor IX prophylaxis therapy**; or**
  - Patient has been determined to be an appropriate candidate for Hemgenix by the Hemophilia Treatment Center based on willingness to adhere to initial and long-term monitoring and management;

  and

- Patient has had a minimum of 150 exposure days to a Factor IX agent; **and**
- Patient does not have a history of inhibitors to Factor IX greater than or equal to 0.6 Bethesda units [BU]; **and**
- Patient does not screen positive for active Factor IX inhibitors as defined as greater than or equal to 0.6 Bethesda units [BU] prior to administration of Hemgenix; **and**
- Patient has not gone through Immune Tolerance Induction (ITI); **and**
- Liver health assessments including enzyme testing [alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin)] and hepatic ultrasound and elastography are performed to rule out radiological liver abnormalities and/or sustained liver enzyme elevations; **and**
- **All** of the following:
  - Documentation that the patient has been evaluated for the presence of preexisting neutralizing antibodies to the adenovirus vector (e.g., AAV-5) used to deliver the therapy; **and**
  - Patient has had pre-existing anti-AAV5 neutralizing antibodies measured through the laboratory developed, CLIA-validated AAV5 Neutralizing Antibody Test made available through CSL Behring; **and**
  - The patient does not have high anti-AAV antibody (e.g., AAV-5) titers that may be associated with a lack of response to treatment based on published clinical evidence;

  and
- **One** of the following:
  - Patient is not HIV positive; **or**
  - Patient is HIV positive and is virally suppressed with anti-viral therapy (i.e., < 200 copies of HIV per mL);

  and
- The patient's hepatitis B surface antigen is negative; **and**
- **One** of the following:
  - Patient's hepatitis C virus (HCV) antibody is negative; **or**
  - Patient's HCV antibody is positive and the patient's HCV RNA is negative;

  and
- The patient is not currently using antiviral therapy for hepatitis B or C; **and**
- Patient has not previously received treatment with Hemgenix (etranacogene dezaparvovec-drlb); **and**
- Hemgenix is administered within a Hemophilia Treatment Center (HTC) that holds Federal designation as evidenced by being listed within the CDC's HTC directory[11]; **and**
- Hemgenix dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Authorization will be issued for no more than one treatment per lifetime and for no longer than 45 days from approval

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1411	Injection, etranacogene dezaparvovec-drlb, per therapeutic dose

Diagnosis Code	Description
D67	Hereditary factor IX deficiency

Background

Hemophilia B is a genetic bleeding disorder resulting from missing or insufficient levels of blood clotting Factor IX. Most individuals who have Hemophilia B and experience symptoms are men. The prevalence of Hemophilia B in the population is about one in 40,000; Hemophilia B represents about 15% of patients with hemophilia.[2] Treatment typically involves replacing the missing or deficient clotting factor to improve the body's ability to stop bleeding and promote healing. Patients with severe

Hemophilia B typically require a routine treatment regimen of intravenous (IV) infusions of Factor IX replacement products to maintain sufficient levels of clotting factor to prevent bleeding episodes.

The term "gene therapy" usually has been used to describe an ex vivo or in vivo therapy whereby RNA or DNA are introduced into target cells (ex vivo) or tissues (in vivo) by a delivery vector while "cellular therapy" is a broad term that encompasses both the infusion of a cellular product for the purpose of hematopoietic reconstitution and the infusion of a cellular product intended to have a direct immunologic impact.[9] There is a general consensus among the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the American Society of Gene and Cell Therapy (ASGCT) defining gene therapy as changes in gene expression, achieved by replacing or correcting a disease-causing gene, inactivating a target gene, or inserting a new or modified gene, using a vector or delivery system of genetic sequence or gene, genetically modified microorganisms, viruses, or cells.[6,7,8] The rapid growth of cellular and gene therapies over the past few years has revealed the need for an accurate and uniform taxonomy. Work is ongoing across a number of industry stakeholders including clinicians, scientists, payers, and coders to standardize nomenclature regarding what constitutes a cellular therapy or a gene therapy.[9] In the United States, the FDA establishes the regulatory framework for clinical trials and approval of therapeutic agents such as gene and cellular therapy. Specifically, the FDA Center for Biologics Evaluation and Research regulates cellular therapy products and human gene therapy products as biologics, as well as some devices related to cellular and gene therapy.[7]

Hemgenix is a one-time gene therapy product given as a single dose by IV infusion. Hemgenix consists of a viral vector carrying a gene for clotting Factor IX. Specifically, AAV5-hFIXco-Padua (AMT- 061) is a recombinant adeno-associated viral vector of serotype 5 (AAV5) containing the Padua variant of a codon-optimized human FIX complementary deoxyribonucleic acid (cDNA) under the control of a liver-specific promoter.[3] The gene is expressed in the liver to produce Factor IX protein, to increase blood levels of Factor IX and thereby limit bleeding episodes.

Clinical Evidence

Proven

Hemophilia B

The efficacy of Hemgenix was established in an open-label, single-arm study in 54 adult male patients aged 19 to 75 years, with severe or moderately severe Hemophilia B. Patients prospectively completed a lead-in period of at least 6 months with the intent to receive standard of care routine Factor IX prophylaxis. Patients then received a single IV dose of Hemgenix. 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.

The estimated mean ABR during months 7 to 18 after Hemgenix treatment was 1.9 bleeds/year (95% CI: 1.0, 3.4), compared with an estimated mean ABR of 4.1 bleeds/year (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 non-inferiority of ABR during months 7 to 18 compared to the lead-in period. Two patients were not able to stop routine prophylaxis after Hemgenix treatment. In one patient with a preexisting neutralizing anti-AAV5 antibody titer of 1:3212, no human Factor IX expression was observed, and restart of the exogenous Factor IX prophylaxis was needed for bleeding events. In a second patient, an infusion-related hypersensitivity reaction was observed after initiation of administration of Hemgenix and only 10% of the HEMGENIX dose was administered. During months 7 to 18, an additional patient received prophylaxis from days 396 to 534. Warnings and precautions for Hemgenix include infusion reactions, hepatotoxicity, immune mediated neutralization of the AAV5 vector capsid, hepatocellular carcinogenicity, and monitoring laboratory tests. The most common adverse reactions (≥ 5%) with Hemgenix use were elevated alanine aminotransferase, headache, blood creatine kinase elevations, flu-like symptoms, infusion-related reactions, fatigue, malaise, and elevated aspartate aminotransferase.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Hemgenix (etranacogene dezaparvovec-drlb) is FDA-labeled for treatment of adults with Hemophilia B (congenital Factor IX deficiency) who currently use Factor IX prophylaxis therapy, have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.

References

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Policy History/Revision Information

Date	Summary of Changes
11/01/2023	**Coverage Rationale** · Revised coverage criteria; replaced criterion requiring "Hemgenix is *delivered by or in consultation with* a Hemophilia Treatment Center (HTC)" with "Hemgenix is *administered within* a Hemophilia Treatment Center (HTC) *that holds Federal designation as evidenced by being listed within the CDC's HTC directory*" **Supporting Information** · Updated *References* section to reflect the most current information ● Archived previous policy version IEX00120.04

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent

professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.