Clinical Policy: Etranacogene Dezaparvovec-drlb (Hemgenix)

Reference Number: CP.PHAR.580
Effective Date: 11.22.22
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Etranacogene dezaparvovec-drlb (Hemgenix®) is an adeno-associated virus (AAV) vector-based gene therapy.

FDA Approved Indication(s)

Hemgenix is 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.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

All requests reviewed under this policy **require medical director review**.

It is the policy of health plans affiliated with Centene Corporation® that Hemgenix is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Hemophilia B (must meet all)**:**

1. Diagnosis of congenital hemophilia B (factor IX deficiency);
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. Member has severe or moderately severe hemophilia (defined as a factor IX level of ≤ 2%);
5. Member meets one of the following (a, b, or c):
   a. Adherence to current use of a factor IX product* (e.g., Alprolix®, Benefix®, Idelvion®, Ixinity®, Rebinyn®, Rixubis®) for routine prophylaxis as assessed and documented by prescriber;
   b. Have current or historical life-threatening hemorrhage;
   c. Have repeated, serious spontaneous bleeding episodes (*see Appendix D*);
   **Prior authorization may be required*
6. Member has been treated with factor IX product for a minimum of 150 exposure days (*see Appendix D*);

7. Member meets all of the following (a, b, and c):
   a. No previous documented history of a detectable factor IX inhibitor;
   b. Documentation of inhibitor level assay < 0.6 Bethesda units (BU) within the last 12 months;
   c. If member had an initial positive test result for factor IX inhibitor, member has documentation of a subsequent negative test within 2 weeks;
8. Member has had all of the following baseline liver assessments within the last 3 months (a, b, and c):
   a. Documentation of liver enzymes within normal limits (i.e., alanine aminotransferase [ALT], aspartate aminotransferase [AST], alkaline phosphatase [ALP] and total bilirubin);
   b. Documentation of normal hepatic ultrasound and elastography;
   c. If member has evidence of radiological liver abnormalities and/or sustained liver enzyme elevations, attestation from hepatologist that member is eligible for Hemgenix;
9. Member has not received prior gene therapy;
10. Member has been tested for neutralizing anti-adeno-associated virus serotype 5 (AAV5) antibodies and is deemed a suitable candidate for treatment;
11. Documentation of member's body weight in kg;
12. Dose does not exceed 2 x 10^{13} genome copies (gc) per kg.

Approval duration: 3 months (*1 dose only*)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Congenital Hemophilia B

1. Continued therapy will not be authorized as Hemgenix is indicated to be dosed one time only.

Approval duration: Not applicable

B. Other diagnoses/indications

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AAV: adeno-associated virus
ALP: alkaline phosphatase
ALT: alanine aminotransferase
AST: aspartate aminotransferase
BU: Bethesda units
ED: exposure day
FDA: Food and Drug Administration
gc: genome copies

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Factor IX recombinant products for routine prophylaxis		
Alprolix®	50 IU/dL/kg IV once weekly or 100 IU/dL/kg IV once every 10 days	100 IU/dL/kg/dose
BeneFIX®	100 IU/kg IV once weekly	100 IU/kg/dose
Idelvion®	25-40 IU/kg IV every 7 days followed by 50-75 IU/kg IV every 14 days once well-controlled	40 IU/kg/week
Ixinity®	40 to 70 IU/kg IV twice weekly	140 IU/kg/week
Rebinyn®	40 IU/kg IV once weekly	40 IU/kg/week
Rixubis®	40-60 IU/kg IV twice weekly	60 IU/kg/dose

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- Serious bleeding episodes include bleeds in the following sites: intracranial; neck/throat; gastrointestinal; joints (hemarthrosis); muscles (especially deep compartments such as the iliopsoas, calf, forearm), or mucous membranes of the mouth, nose and genitourinary tract.
- Spontaneous bleed is defined as a bleeding episode that occurs without apparent cause and is not the result of trauma.
- Exposure day (ED): An ED is a day on which a person with hemophilia has been infused with factor concentrate to treat or prevent a bleed. The number of EDs consists only of those days on which factor was infused.
    - 150 EDs of cumulative treatment increases the likelihood of immunologic stability – a decreased risk of producing inhibitors. Patients rarely develop inhibitors after 150 EDs.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Hemophilia B	Recommended dose: 2×10^{13} gc/kg of body weight by IV infusion	2×10^{13} gc/kg

VI. Product Availability
Single-dose cell suspension: 10 to 48 single-use vials with a nominal concentration of 1×10^{13} gc/mL with each vial containing an extractable volume of ≥ 10 mL

VII. References
1. Hemgenix Prescribing Information. Kankakee, IL: CSL Behring; November 2022. Available at: https://labeling.cslbehring.com/PI/US/Hemgenix/EN/Hemgenix-Prescribing-Information.pdf. Accessed October 11, 2023.
2. ClinicalTrials.gov. HOPE-B: Trial of AMT-061 in severe or moderately severe hemophilia b patients. Available at: https://clinicaltrials.gov/ct2/show/NCT03569891. Accessed October 30, 2023.
3. Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020 Aug;26 Suppl 6:1-158.
4. Carcao M and Goudemand J. Inhibitors in hemophilia: A primer, 5th edition. World Federation of Hemophilia. Available at: https://www1.wfh.org/publication/files/pdf-1122.pdf.
5. Medical and Scientific Advisory Council (MASAC) of the National Bleeding Disorders Foundation (formerly National Hemophilia Foundation): Database of treatment guidelines. Available at: https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents. Accessed October 26, 2023.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	04.05.22	05.22
Template changes applied to other diagnoses/indications	09.19.22	
Drug is now FDA approved – criteria updated per FDA labeling: clarified that documentation is required for inhibitor level assay; added criterion for subsequent negative factor IX inhibitor test if member has an initial positive test result for factor IX inhibitors per PI; added criteria for normal baseline liver assessments and hepatologist attestation of Hemgenix eligibility if sustained liver enzymes or radiological liver abnormalities present per PI; added factor IX recombinant products for routine prophylaxis in Appendix B; added criterion that member has not received prior gene therapy; added neutralizing anti-AAV5 antibodies information to Appendix D; updated sites of serious bleeds per WHF guideline in Appendix D; references reviewed and updated.	11.30.22	02.23
Added HCPCS code [J1411].	04.17.23	
1Q 2024 annual review: no significant changes; references reviewed and updated.	10.30.23	02.24
Revised baseline severity and treatment history criteria from use of a factor IX product for ≥ 12 months with ≥ 1 serious spontaneous bleed to current use of a factor IX product with timeframe removal, added option of current or historical life-threatening hemorrhage, and modified option of repeated, serious spontaneous bleeding episodes to align with FDA; revised criterion for AAV5 neutralizing antibody titer of ≤ 1:678 to instead require a neutralizing anti-AAV5 antibody test and that member is deemed a suitable candidate for treatment due to the evolving nature of the anti-AAV5 neutralizing antibody test; added requirement for documentation of member's body weight for dose determination.	07.22.24	11.24

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional

organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.