Clinical Policy: Etranacogene Dezaparvovec-drlb (Hemgenix)

Reference Number: PA.CP.PHAR.580
Effective Date: 01/2023
Last Review Date: 01/2023

Revision Log

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 PA Health & Wellness® 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 both of the following (a, b or c):
   a. Member has been adherent with use of a factor IX product* (e.g., Alprolix®, Benefix®, Idelvion®, Ixinity®, Rebinyn®, Rixubis®) for routine prophylaxis for at least 12 months as assessed and documented by prescriber;
   b. Occurrence of at least one serious spontaneous bleeding event;
   c. Current of history of life threatening hemorrhage;
   **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 documentation of AAV5 neutralizing antibody titer ≤ 1:678;
11. Dose does not exceed 2 x 10^{13} genome copies (gc) per kg.

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

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53.

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.
- In the clinical studies with Hemgenix, an unvalidated clinical trial assay was utilized to assess preexisting neutralizing anti-AAV5 antibodies. The subject sub-group with detectable preexisting neutralizing anti-AAV5 antibodies up to titers of 1:678 showed mean factor IX activity that was numerically lower compared to that subject sub-group without detectable preexisting neutralizing anti-AAV5 antibodies. Subjects, with and without preexisting neutralizing anti-AAV5 antibodies, demonstrated hemostatic protection. In one subject 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.
    - Patients who intend to receive treatment with Hemgenix are encouraged to enroll in a study to measure pre-existing anti-AAV5 neutralizing antibodies by calling CSL Behring at 1-800-504-5434. The study evaluates the effect of pre-existing anti-AAV5 neutralizing antibodies on the risk of bleeding.

V. Dosage and Administration

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

VI. Product Availability

Single-dose cell suspension: 10 to 48 single-use vials with a nominal concentration of 1 x 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 November 23, 2022.
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 November 30, 2022.
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.

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
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01/2023	