Neighborhood Health Plan OF RHODE ISLAND™
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Hemgenix® (etranacogene dezaparvovec-drlb)
(Intravenous)

Effective Date: 5/1/2023
Review Date: 3/30/2023, 12/07/2023, 01/04/2024, 3/27/2024, 08/14/2024, 09/17/2025

Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Coverage will be provided for one dose and may not be renewed.

II. Dosing Limits

A. Max Units (per dose and over time) [HCPCS Unit]:

- 1 kit (based on weight chart below)

III. Summary of Evidence

Hemgenix (etranacogene dezaparvovec) is a one-time weight-based gene therapy indicated for the treatment of adults with Hemophilia B (congenital factor IX [FIX] deficiency) who currently use FIX prophylaxis therapy or have current or historical life-threatening hemorrhage or have repeated, serious spontaneous bleeding episodes. Hemophilia B is an X-linked genetic bleeding disorder that results from missing or insufficient levels of FIX. The clinical efficacy of Hemgenix was evaluated in HOPE-B, a phase 3, open-label clinical trial with 54 patients. A 54% reduction in annualized bleeding rates (ABR) was demonstrated with a mean ABR of 4.1 during the lead-in period (first 6 months) to a mean ABR of 1.9 during months 7 to 18 after Hemgenix treatment. The most common side effects, occurring in over 5% of patients in the trial were liver enzyme elevations, headache, mild infusion-related reactions, and flu-like symptoms. In the trial, 94% of patients treated with Hemgenix discontinued use of prophylaxis and remained free of previous continuous routine prophylaxis therapy.

IV. Initial Approval Criteria [1-13]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

Hemophilia B (Congenital Factor IX Deficiency) † Φ

- Patient is at least 18 years of age; **AND**
- Hemgenix must be prescribed by, or consultation with a hematologist; **AND**
- Patient will undergo treatment at a manufacturer approved Qualified Treatment Center (QTC); **AND**
- Patient has a diagnosis of moderately severe or severe congenital factor IX deficiency (i.e., ≤2% of normal circulating factor IX), as confirmed by blood coagulation testing, for which the subject is on continuous routine factor IX prophylaxis, unless there is a contraindication or intolerance*(Note: Continuous routine prophylaxis is defined as the intent of treating with an a priori defined frequency of infusions (e.g., twice weekly, once every two weeks, etc.) as documented in the medical records)*; **AND**
- Patient has not received prior hemophilia AAV-vector–based gene therapy; **AND**
- Patient has one or more of the following:
    - Currently use Factor IX prophylaxis therapy (e.g., AlphaNine SD, Alprolix, BeneFIX, Idelvion, Ixinity, Mononine, Profilnine, Rebinyn, Rixubis, etc.); **OR**
    - Have current or historical life-threatening hemorrhage; **OR**
    - Have repeated, serious spontaneous bleeding episodes, *(e.g., intramuscular hematomas requiring hospitalization, hemarthrosis, central nervous system (CNS) bleeding (including intracranial hemorrhage), pulmonary hemorrhage, life-threatening gastrointestinal (GI) hemorrhage and umbilical cord bleeding)*; **AND**
- Patient has been tested and found negative for Factor IX inhibitor titers, (i.e., <0.6 Bethesda Units) and does not have a prior history of inhibitors (if test result is positive, re-test within approximately 2 weeks. If re-test is also positive, Hemgenix should not be given); **AND**
- Patient Factor IX activity will be monitored periodically (e.g., weekly for 3 months) as well as presence of inhibitors if bleeding is not controlled (Note: patients will continue to require exogenous Factor IX until response to Hemgenix occurs) ; **AND**
- Patient will discontinue Factor IX prophylaxis therapy upon achieving FIX levels of 5% from Hemgenix (etranacogene dezaparvovec) treatment; **AND**
- Patient has been screened for anti-AAV5 antibody titers and has been deemed a suitable candidate for treatment *(Note: This assay was used in the HOPE-B clinical trial and is assessable via CSL Behring)*; **AND**
- Patient will have baseline liver function assessed prior to and after therapy; according to the monitoring schedule outlined in the product labeling with corticosteroids administered in response to elevations; **AND**
- Patients with preexisting risk factors for hepatocellular carcinoma (e.g., patients with cirrhosis, advanced hepatic fibrosis, hepatitis C or B, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption, non-alcoholic steatohepatitis (NASH), and advanced age) will have abdominal ultrasound screenings and be monitored regularly (e.g., annually) for alpha-fetoprotein (AFP) elevations following administration

Notes:

- It may take several weeks before improved hemostatic control becomes apparent after Hemgenix (etranacogene dezaparvovec) infusion; therefore, continued hemostatic support with exogenous human Factor IX may be needed during the first weeks after Hemgenix (etranacogene dezaparvovec) infusion.

• Use of exogenous Factor IX concentrates before and after Hemgenix (etranacogene dezaparvovec) administration may impede assessment of endogenous, Hemgenix (etranacogene dezaparvovec)-derived Factor IX activity.

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); Φ Orphan Drug

V. Renewal Criteria

Coverage cannot be renewed.

VI. Dosage/Administration

Indication	Dose
Hemophilia B (Congenital Factor IX Deficiency	The recommended dose of Hemgenix 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. Calculate the dose as follows: – Hemgenix dose (in mL) = patient body weight (in kilogram) x 2 *The multiplication factor 2 represents the per kilogram dose (2×10^{13} gc/kg) divided by the amount of genome copies per mL of the Hemgenix solution (1×10^{13} cg/mL).* – Number of Hemgenix vials needed = Hemgenix dose (in mL) divided by 10 (round up to next whole number of vials). *The division factor 10 represents the extractable volume of Hemgenix from each vial (10 mL).*
• Prepare Hemgenix using sterile technique under aseptic conditions, proper engineering controls (e.g., biological safety cabinet or isolator) and according to institutional policies. • Do not expose Hemgenix to the light of an ultraviolet radiation disinfection lamp. • Confirm that the patient's identity matches with the patient-specific identifier number on the outer carton. • Verify the required dose of Hemgenix based on the patient's body weight. • Confirm that the carton contains sufficient number of vials to prepare the diluted Hemgenix patient-specific infusion bag. • Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. • For single-dose intravenous infusion only. • DO NOT administer Hemgenix as an intravenous push or bolus. • DO NOT infuse the diluted Hemgenix solution in the same intravenous line with any other products. • DO NOT use a central line or port.	

VII. Billing Code/Availability Information

HCPCS code:

- J1411 Injection, etranacogene dezaparvovec-drlb, per therapeutic dose; 1 billable unit = 1 kit (based on weight chart below)

NDC:

Hemgenix kit sizes:

Total number of vials	Patient Weight (kg)	Total Volume (mL)	NDC
10	46-50	100	00053-0100-10
11	51-55	110	00053-0110-11
12	56-60	120	00053-0120-12

13	61-65	130	00053-0130-13
14	66-70	140	00053-0140-14
15	71-75	150	00053-0150-15
16	76-80	160	00053-0160-16
17	81-85	170	00053-0170-17
18	86-90	180	00053-0180-18
19	91-95	190	00053-0190-19
20	96-100	200	00053-0200-20
21	101-105	210	00053-0210-21
22	106-110	220	00053-0220-22
23	111-115	230	00053-0230-23
24	116-120	240	00053-0240-24
25	121-125	250	00053-0250-25
26	126-130	260	00053-0260-26
27	131-135	270	00053-0270-27
28	136-140	280	00053-0280-28
29	141-145	290	00053-0290-29
30	146-150	300	00053-0300-30
31	151-155	310	00053-0310-31
32	156-160	320	00053-0320-32
33	161-165	330	00053-0330-33
34	166-170	340	00053-0340-34
35	171-175	350	00053-0350-35
36	176-180	360	00053-0360-36
37	181-185	370	00053-0370-37
38	186-190	380	00053-0380-38
39	191-195	390	00053-0390-39
40	196-200	400	00053-0400-40
41	201-205	410	00053-0410-41
42	206-210	420	00053-0420-42
43	211-215	430	00053-0430-43
44	216-220	440	00053-0440-44
45	221-225	450	00053-0450-45
46	226-230	460	00053-0460-46
47	231-235	470	00053-0470-47
48	236-240	480	53-480-48

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

VIII. References

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3. Guidelines for the Management of Hemophilia. 3rd Edition. World Federation of Hemophilia 2020. Available at: https://www1.wfh.org/publications/files/pdf-1863.pdf. Accessed May 2024.
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6. Mingot-Castellano, et al. Application of Pharmacokinetics Programs in Optimization of Haemostatic Treatment in Severe Hemophilia a Patients: Changes in Consumption, Clinical Outcomes and Quality of Life. Blood. 2014 December; 124 (21).
7. MASAC RECOMMENDATION CONCERNING PROPHYLAXIS FOR HEMOPHILIA A AND B WITH AND WITHOUT INHIBITORS. National Hemophilia Foundation. MASAC Document #267 (Replaces Document #241); March 2022. Available at: https://www.bleeding.org/sites/default/files/document/files/267_Prophylaxis.pdf. Accessed May 2024.
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11. Pipe S, van der Valk P, Verhamme P, et al. Long-term bleeding protection, sustained FIX activity, reduction of FIX consumption and safety of hemophilia B gene therapy: results from the HOPE-B trial 3 years after administration of a single dose of etranacogene dezaparvovec in adult patients with severe or moderately severe hemophilia B. *Blood* (2023) 142 (Supplement 1): 1055. https://doi.org/10.1182/blood-2023-187624
12. MASAC Recommendations on Hemophilia Treatment Center Preparedness for Delivering Gene Therapy for Hemophilia. National Hemophilia Foundation. MASAC Document #282. October 2023. Available at: https://www.bleeding.org/healthcare-professionals/guidelines-on-care/masac-documents/masac-document-282-masac-recommendations-on-hemophilia-treatment-center-preparedness-for-delivering-gene-therapy-for-hemophilia. Accessed May 2024.
13. Thornburg, C.D., Simmons, D.H., von Drygalski, A. Evaluating gene therapy as a potential paradigm shift in treating severe hemophilia. BioDrugs. 2023. DOI: 10.1007/s40259-023-00615-4.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D67	Hereditary factor IX deficiency

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/ search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Hemgenix was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Hemgenix to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.