UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hemophilia – Gene Therapy – Hemgenix Utilization Management Medical Policy
- Hemgenix® (etranacogene dezaparvovec-drlb intravenous infusion – CSL Behring and uniQure)

REVIEW DATE: 02/11/2026; selected revision 02/25/2026

OVERVIEW

Hemgenix, an adeno-associated virus (AAV) vector-based gene therapy, is indicated for the treatment of adults with **hemophilia B** (congenital Factor IX deficiency) who: 1) currently use Factor IX prophylaxis therapy; or 2) have current or historical life-threatening hemorrhage; or 3) have repeated, serious spontaneous bleeding episodes.[1] The recommended dose of Hemgenix is 2 x 10^{13} genome copies per kg of body weight given as a one-time (per lifetime) single dose as an intravenous infusion.

Disease Overview

Hemophilia B is a genetic bleeding disorder caused by missing or insufficient levels of blood Factor IX, a protein required to produce blood clots to halt bleeding.[2-4] The condition is a rare X-linked bleeding disorder that mainly impacts males. The prevalence of hemophilia B in males is one in 30,000 live births.[4] Symptoms include heavy or prolonged bleeding following an injury or trauma, after a medical or dental procedure, or post-surgery.[2-4] Bleeding can also occur internally into joints, muscles, or internal organs. Spontaneous bleeding events may also occur. Complications in patients with hemophilia B include joint disease and hemarthrosis.[2-4] For a patient with hemophilia B, bleeding episodes may be more common in childhood and adolescence compared with adulthood.[2] There is a strong correlation between Factor IX levels and bleeding severity. Normal plasma levels of Factor IX range from 50% to 150%.[3] The disease is classified based on reduced levels. Mild, moderate, and severe hemophilia B is characterized by Factor IX levels ranging from 6% up to 49%, 1% up to 5%, and < 1%, respectively.[3] In general, a patient with factor IX clotting activity > 40% usually had normal coagulation.[2] Other therapies used in the management of hemophilia B involve Factor IX products administered intravenously (both recombinant and plasma-derived) which are used routinely to prevent bleeding or are given on-demand to treat bleeding episodes associated with hemophilia B.[2] Also, non-factor prophylactic agents given by subcutaneous (SC) injection are also available for use in patients ≥ 12 years of age (i.e., Qfitlia™ [fitusiran SC injection], Hympavzi® [marstacimab SC injection], and Alhemo® [concizumab SC injection]).

Clinical Efficacy

The efficacy of Hemgenix was assessed in a prospective, open-label, single-dose, single-arm, multinational pivotal study called HOPE-B that involved 54 adult males with moderately severe or severe hemophilia B (Factor IX levels ≤ 2%).[1,5] Patients prospectively completed a lead-in period of at least 6 months in which standard care routine Factor IX prophylaxis therapy was given. This was followed by a single intravenous dose of Hemgenix. Patients were permitted to continue Factor IX prophylaxis during Months 0 to 6 after dosing, if needed, until Factor IX levels were adequate. Prior to screening, patients had been on stable prophylactic therapy for at least 2 months and had greater than 150 exposure days of treatment with a Factor IX product.[5] Factor IX inhibitors (or a history), uncontrolled human immunodeficiency virus (HIV) infection, or advanced liver fibrosis prevented participation. Adequate hepatic and renal function were required. The estimated mean annualized bleeding rate during Months 7 to 18 following Hemgenix treatment was 1.9 bleeds/year compared with 4.1 bleeds/year during the lead-in period (before Hemgenix administration).[1] At 18 months after treatment, Factor IX activity had increased by 34.3%.[5] At the final 5-year follow-up, the annualized bleeding rate for all bleeding events was 1.52 bleeds/year during Months 7 through 60 after administration of Hemgenix.[6] At this timepoint, the mean Factor IX activity level was

© 2026. All Rights Reserved.
This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

36.1% and the mean exogenous Factor IX consumption for routine prophylaxis and treatment of bleeding events had decreased by 96%.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Hemgenix. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Hemgenix as well as the monitoring required for adverse events and long-term efficacy, approval requires Hemgenix to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one-time (per lifetime) as a single dose. The approval duration is 90 days to allow for an adequate timeframe to prepare and administer one dose of therapy. If claims history is available, verification is required for certain criteria as noted by **[verification in claims history required]**. For the dosing criteria, verification of the appropriate weight-based dosing is required by a Medical Director as noted by **[verification required]**. In the criteria for Hemgenix, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: males are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression. All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation.

Some clients have elected Embarc Benefit Protection. For these clients, the Medical Director will coordinate with EviCore to ensure the Embarc Benefit Protection portion of the review has been completed. If the Embarc Benefit Protection portion of the review has not been completed, the Medical Director will route to Embarc@eviCore.com prior to completing the review.

Documentation: Documentation is required for use of Hemgenix as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Hemgenix is recommended in those who meet the following criteria:

FDA-Approved Indication

---

1. **Hemophilia B.** Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, I, J, K, L, M, N, and O):
   - **A)** Patient is male*; AND
   - **B)** Patient is ≥ 18 years of age; AND
   - **C)** Patient has not received a gene therapy for hemophilia B in the past **[verification in claims history required]**; AND
     Note: If no claim for Hemgenix or Beqvez (fidanacogene elaparvovec-dzkt intravenous infusion) is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Hemgenix or Beqvez.
   - **D)** Patient has moderately severe or severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level ≤ 2% of normal **[documentation required]**; AND
   - **E)** Patient meets ONE of the following (i, ii, or iii):

© 2026. All Rights Reserved.
This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

- **i.** According to the prescribing physician, the patient has a history of use of Factor IX therapy for ≥ 150 exposure days; OR
- **ii.** Patient meets BOTH of the following (a and b):
  - **a)** Patient has a history of life-threatening hemorrhage; AND
  - **b)** On-demand use of Factor IX therapy was required for this life-threatening hemorrhage; OR
- **iii.** Patient meets BOTH of the following (a and b):
  - **a)** Patient has a history of repeated, serious spontaneous bleeding episodes; AND
  - **b)** On-demand use of Factor IX therapy was required for these serious spontaneous bleeding episodes; AND

F) Patient meets BOTH of the following (i and ii):
- **i.** Factor IX inhibitor titer testing has been performed within the past 30 days **[documentation required]**; AND
- **ii.** Patient is negative for Factor IX inhibitors **[documentation required]**; AND

G) Patient meets BOTH of the following (i and ii):
- **i.** Patient does not have an active infection with hepatitis B virus or hepatitis C virus **[documentation required]**; AND
- **ii.** Patient is not currently receiving antiviral therapy for a prior hepatitis B virus or hepatitis C virus exposure **[documentation required]**; AND

H) According to the prescribing physician, the patient does not have uncontrolled human immunodeficiency virus infection; AND

I) Patient has undergone liver function testing within the past 30 days and meets ALL of the following (i, ii, iii, and iv):
- **i.** Alanine aminotransferase level is ≤ two times the upper limit of normal **[documentation required]**; AND
- **ii.** Aspartate aminotransferase level is ≤ two times the upper limit of normal **[documentation required]**; AND
- **iii.** Total bilirubin level is ≤ two times the upper limit of normal **[documentation required]**; AND
- **iv.** Alkaline phosphatase level is ≤ two times the upper limit of normal **[documentation required]**; AND

J) Patient does not have evidence of advanced liver impairment and/or advanced fibrosis; AND

K) Within the past 30 days, the platelet count was ≥ 50 x 10^9/L **[documentation required]**; AND

L) Within the past 30 days, patient meets ONE of the following (i or ii):
- **i.** Patient has an estimated creatinine clearance ≥ 30 mL/min **[documentation required]**; OR
- **ii.** Creatinine level is ≤ two times the upper limit of normal **[documentation required]**; AND

M) The medication is prescribed by a hemophilia specialist physician; AND

N) Current patient body weight has been obtained within the past 30 days **[documentation required]**; AND

O) If criteria A through N are met, approve one dose (kit) of Hemgenix to provide for a one-time (per lifetime) single dose of 2 x 10^{13} genome copies per kg of body weight by intravenous infusion **[verification required]**. Table 1 provides the kit size and the National Drug Codes (NDCs).

* Refer to the Policy Statement.

Dosing. The recommended dose of Hemgenix is a one-time (per lifetime) single dose of 2 x 10^{13} genome copies per kg of body weight by intravenous infusion.

© 2026. All Rights Reserved.
This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Hemgenix is not recommended in the following situations:

1. **Prior Receipt of Gene Therapy.** Prior receipt of gene therapy was a reason for patient exclusion in the pivotal study.

2. **Patient with a History of Factor IX Inhibitors.** A history of Factor IX inhibitors was a reason for patient exclusion in the pivotal trial.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Table 1. Hemgenix Multi-Vial Kits.[1]

Total Number of Vials per Kit	Patient Body Weight	Total Volume per Kit	NDC Number
10	46 to 50 kg	100	0053-0100-10
11	51 to 55 kg	110	0053-0110-11
12	56 to 60 kg	120	0053-0120-12
13	61 to 65 kg	130	0053-0130-13
14	66 to 70 kg	140	0053-0140-14
15	71 to 75 kg	150	0053-0150-15
16	76 to 80 kg	160	0053-0160-16
17	81 to 85 kg	170	0053-0170-17
18	86 to 90 kg	180	0053-0180-18
19	91 to 95 kg	190	0053-0190-19
20	96 to 100 kg	200	0053-0200-20
21	101 to 105 kg	210	0053-0210-21
22	106 to 110 kg	220	0053-0220-22
23	111 to 115 kg	230	0053-0230-23
24	116 to 120 kg	240	0053-0240-24
25	121 to 125 kg	250	0053-0250-25
26	126 to 130 kg	260	0053-0260-26
27	131 to 135 kg	270	0053-0270-27
28	136 to 140 kg	280	0053-0280-28
29	141 to 145 kg	290	0053-0290-29
30	146 to 150 kg	300	0053-0300-30
31	151 to 155 kg	310	0053-0310-31
32	156 to 160 kg	320	0053-0320-32
33	161 to 165 kg	330	0053-0330-33
34	166 to 170 kg	340	0053-0340-34
35	171 to 175 kg	350	0053-0350-35
36	176 to 180 kg	360	0053-0360-36
37	181 to 185 kg	370	0053-0370-37
38	186 to 190 kg	380	0053-0380-38
39	191 to 195 kg	390	0053-0390-39
40	196 to 200 kg	400	0053-0400-40
41	201 to 205 kg	410	0053-0410-41
42	206 to 210 kg	420	0053-0420-42
43	211 to 215 kg	430	0053-0430-43
44	216 to 220 kg	440	0053-0440-44
45	221 to 225 kg	450	0053-0450-45
46	226 to 230 kg	460	0053-0460-46
47	231 to 235 kg	470	0053-0470-47
48	236 to 240 kg	480	0053-0480-48

NDC – National Drug Code.

REFERENCES

© 2026. All Rights Reserved.
This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

1. Hemgenix® intravenous infusion [prescribing information]. King of Prussia, PA; Kankakee, IL; and Lexington, MA: CSL Behring and uniQure; November 2022.
2. Konkle BA, Nakaya Fletcher S. Hemophilia B. 2000 Oct 2 [Updated 2025 Aug 7]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026.
3. National Bleeding Disorders Foundation. Hemophilia B. An overview of symptoms, genetics, and treatments to help you understand hemophilia B. Available at: https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b. Accessed on February 8, 2026.
4. Chowdary P, Carcao M, Kenet G, Pipe SW. Haemophilia. *Lancet*. 2025;405:736-750.
5. Pipe SW, Leebeek FWG, Recht M, et al. Gene therapy with etranacogene dexaparvovec for hemophilia B. *N Engl J Med*. 2023;388:706-718.
6. Pipe SW, Miesbach W, Recht M, et al, for the HOPE-B study group investigators. Final analysis of the study of etranacogene dezaparvovec for hemophilia B. *N Engl J Med*. 2026;394:463-474.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Hemophilia B:** An overview of the changes are described below. • The documentation requirement was removed regarding the criterion that the "Patient does not have evidence of advanced liver impairment and/or advanced fibrosis". • The following criteria were removed which stated that after the Hemgenix infusion, the physician attests that the following will be performed: 1) liver enzyme testing to monitor for liver enzyme elevations will be done at least weekly for the first 3 months and periodically thereafter; AND implementing a course of corticosteroids will be considered if the patient experiences clinically relevant increases in alanine aminotransferase levels; 2) the patient will undergo monitoring for Factor IX activity at least weekly for the first 3 months and periodically thereafter; and 3) the patient with preexisting risk factors for hepatocellular carcinoma will receive abdominal ultrasound screenings and be monitored at least annually for alpha fetoprotein elevations in the 5 years following receipt of Hemgenix. • The requirement for the specialist physician was changed from "physician who specializes in hemophilia" to "hemophilia specialist physician". • The criterion regarding a current patient body weight be obtained within 30 days was moved to a separate criterion. Previously, this requirement was combined with the Dosing. • Dosing was clarified with emphasis that Hemgenix is given as a "single dose". Also, "documentation required" was replaced with "verification required". A related sentence was added to the Policy Statement that verification of the appropriate weight-based dosing is required by the Medical Director. • Regarding use of Hemgenix in the past, the phrase "verification required by prescriber" was changed to "verification in claims history required". A qualifier was added to reflect that this requirement applies only if a claims history is available; this change was also reflected in the related Policy Statement. Wording regarding "prescriber must attest" was changed to "prescribing physician confirms" regarding the verification that the patient has not previously received Hemgenix. Also, in the Note, the following statement was removed as it is duplicative: verify through claims history that the patient has not previously received Hemgenix. • The phrase "prescriber attests" was removed from the requirement that "prophylactic therapy with Factor IX will not be given after Hemgenix administration once adequate Factor IX levels have been achieved" as well as the to the requirement regarding "patient does not have another coagulation disorder, besides hemophilia B". • In the requirement that Factor IX inhibitor titer testing has been performed "within 30 days", the phrase "before receipt of Hemgenix" was removed. • The phrase regarding liver "health assessment" was changed to liver "function testing". • For the requirement that the patient does not have uncontrolled human immunodeficiency virus, the word "infection" was added after this phrase. **Conditions Not Recommended for Approval:** The condition of "Prior Receipt of Gene Therapy" was added.	02/28/2024

HISTORY (CONTINUED)

Type of Revision	Summary of Changes	Review Date

© 2026. All Rights Reserved.
This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

Selected Revision	**Hemophilia B:** ● Regarding use of Hemgenix in the past, the criterion was changed due to the recent approval of Beqvez (fidanacogene elaparvovec intravenous infusion) for this indication. It now states that the patient has not received "a gene therapy for hemophilia B" in the past. It was added that there should not be claims present for Beqvez and that if claims history is not available, the prescribing physician confirms that the patient has not previously received Beqvez (previously, this only addressed Hemgenix). ● The option of approval was removed that the patient has been receiving routine prophylaxis with Factor IX therapy continuously for ≥ 2 months. ● The requirement that the patient does not currently have an inhibitor to Factor IX was reworded to state that the patient is negative for Factor IX inhibitors. ● The caveat of "According to the prescribing physician" was added to the requirement that the patient does not have uncontrolled human immunodeficiency virus infection; the documentation requirement was removed from this requirement; and the Note that addressed specific laboratory factors was removed. ● The requirement that within 30 days the patient has an estimated creatinine clearance ≥ 30 mL/min AND that the creatinine level is ≤ two times the upper limit of normal was changed to having to meet <u>one</u> of these elements (not both). ● The requirement that the patient does not have another coagulation disorder, besides hemophilia B, was removed.	05/15/2024
Annual Revision	**Hemophilia B:** The requirement that the patient does not have a history of Factor IX inhibitors (with documentation required) was removed from this section. The requirement that prophylactic therapy with Factor IX will not be given after Hemgenix administration once adequate Factor IX levels have been achieved was removed, along with the related Note. The Note that provides examples of advanced liver impairment and/or advanced fibrosis was removed. However, the criterion that the patient does not have evidence of advanced liver impairment and/or advanced fibrosis remains. **Conditions Not Recommended for Approval:** The condition of "Patient with a History of Factor IX Inhibitors" was added to this section. Previously, this was in a criterion related to the diagnosis of hemophilia B.	02/26/2025
Annual Revision	No criteria changes.	02/11/2026
Selected Revision	In the Policy Statement, the following was added: The approval duration is 90 days to allow for an adequate timeframe to prepare and administer one dose of therapy.	02/25/2026

© 2026. All Rights Reserved.
This document is confidential and proprietary. Unauthorized use and distribution are prohibited.