GENE THERAPIES FOR HEMOPHILIA B
BEQVEZ™ (fidanacogene elaparvovec-dzkt)
HEMGENIX® (etranacogene dezaparvovec-hyphendrlb)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for gene therapy for hemophilia B with Beqvez or Hemgenix. By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Hemophilia B is a rare hereditary bleeding disorder caused by deficiency of coagulation factor IX, it is an X-linked recessive disorder primarily affecting males. People with hemophilia B are at risk for excessive and recurrent spontaneous and/or post-traumatic bleeding, which can be life-threatening, particularly in those with severe disease.

Beqvez is a one-time adeno-associated virus vector-based gene therapy indicated for the treatment of adults with moderate to severe hemophilia B (congenital factor IX deficiency) who:

- Are currently receiving routine factor IX prophylaxis therapy, or
- Have a current or historical life-threatening hemorrhage, or
- Have a history of serious spontaneous bleeding episodes, and
- Do not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test.

Beqvez uses a modified adeno-associated virus vector to package a functional factor IX transgene encoding a high-activity factor IX variant to the patient, preferentially targeting the liver where clotting factor IX is produced. The efficacy of Beqvez was evaluated in an ongoing, prospective, open-label, single-arm, multi-national study (N= 45) which enrolled adult male patients with moderately severe to severe hemophilia B (≤ 2% of normal circulating factor IX). A single intravenous infusion of Beqvez results in cell transduction an increase in circulating factor IX activity, and a reduction in annualized bleeding rate in patients with hemophilia B.

Hemgenix is a one-time adeno-associated virus vector-based gene therapy indicated for the treatment of adults with hemophilia B (congenital factor IX deficiency) who:

- Are currently receiving routine factor IX prophylaxis therapy, or
- Have a current or historical life-threatening hemorrhage, or
- Have a history of serious spontaneous bleeding episodes.

With Hemgenix, the factor IX-Padua gene is contained within an adeno-associated viral vector serotype 5 (AAV5) used to introduce a functional copy of the F9 gene into a patient's hepatocytes. The efficacy of

Hemgenix was evaluated in a prospective, open-label, single-dose, single arm, multi-national study (N = 54) which enrolled adult males with severe or moderately severe Hemophilia B (≤ 2% of normal circulating factor IX). A single infusion with Hemgenix results in cell transduction and offers elevated and sustained factor IX levels, a decreased need for routine factor IX prophylaxis, and a reduction in annualized bleeding rate in patients with hemophilia B.

CLINICAL GUIDELINE

Coverage decisions for the use of gene therapy for hemophilia B will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage decisions are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

I. Treatment with Beqvez will be considered medically necessary when ALL of the following criteria are met:

A. The individual is 18 years of age or older; **AND**
B. The individual has severe or moderately severe factor IX deficiency (≤ 2% of normal circulating factor IX); **AND**
C. Treatment is prescribed by or in consultation with a hematologist; **AND**
D. The individual has not previously received gene therapy for hemophilia B; **AND**
E. The individual meets one of the following criteria:
    a. The individual is currently using factor IX prophylaxis; **OR**
    b. The individual has a current or history of a life-threatening hemorrhage; **OR**
    c. The individual has a history of repeated, serious spontaneous bleeding episodes; **AND**
F. The individual has not had a positive factor IX inhibitor test (≥0.6 Bethesda Units [BU]) within the last 30 days or any history of inhibitors to factor IX; **AND**
G. The individual does not have serological evidence of HIV1 or HIV2 infection with either CD4+ cell count ≤ 200 mm3 and/or a viral load >20 copies/mL; **AND**
H. The individual does not have an active infection of Hepatitis B virus or Hepatitis C virus; **AND**
I. The individual is not on antiviral therapy for Hepatitis B virus or Hepatitis C virus infection; **AND**
J. The individual does not have a history of significant liver or biliary disease, and has had all liver health assessments performed as outlined in the prescribing information and procedure section below; **AND**
K. The provider will follow all FDA recommendations for dosage, preparation, administration, monitoring and patient education; **AND**
L. The individual does not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test.

II. Treatment with Hemgenix will be considered medically necessary when ALL of the following criteria are met:

A. The individual is 18 years of age or older; **AND**
B. The individual has severe or moderately severe factor IX deficiency (≤ 2% of normal circulating factor IX); **AND**

C. Treatment is prescribed by or in consultation with a hematologist; **AND**
D. The individual has not previously received gene therapy for hemophilia B; **AND**
E. The individual meets one of the following criteria:
    a. The individual is currently using factor IX prophylaxis; OR
    b. The individual has a current or history of a life-threatening hemorrhage; OR
    c. The individual has a history of repeated, serious spontaneous bleeding episodes; **AND**
F. The individual has not had a positive factor IX inhibitor test (≥0.6 Bethesda Units [BU]) within the last 30 days or any history of inhibitors to factor IX; **AND**
G. The individual does not have serological evidence of HIV1 or HIV2 infection with either CD4+ cell count ≤ 200 mm3 and/or a viral load >20 copies/mL; **AND**
H. The individual does not have an active infection of Hepatitis B virus or Hepatitis C virus; **AND**
I. The individual is not on antiviral therapy for Hepatitis B virus or Hepatitis C virus infection; **AND**
J. The individual does not have a history of significant liver or biliary disease, and has had all liver health assessments performed as outlined in the prescribing information and procedure section below; **AND**
K. The provider will follow all FDA recommendations for dosage, preparation, administration, monitoring and patient education.

Investigational and Not Medically Necessary

Beqvez and Hemgenix are considered investigational and therefore not medically necessary for all other indications.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization of gene therapy for the treatment of hemophilia B with Beqvez or Hemgenix is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for Beqvez:
1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program Gene Therapy for Hemophilia B Prior Authorization Request form (to include physician's order and signature);
2. Clinical documentation supporting the medical necessity of treatment with Beqvez including the following:
    a. Testing confirming severe or moderately severe factor IX deficiency (≤ 2% of normal circulating factor IX);

b. Negative factor IX inhibitor test dated within the previous 30 days;
c. Laboratory testing confirming absence of uncontrolled HIV infection;
d. Liver health assessments including:
    i. Liver function tests confirming absence of significant liver disease;
    ii. Laboratory testing confirming absence of active hepatitis B virus or hepatitis C virus infection;
    iii. Elastography and/or ultrasound and other laboratory assessments for liver fibrosis;
e. Negative test for antibodies to AAVRh74var; AND

3. Other information as requested.

The following information is needed to review requests for Hemgenix:

1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program Gene Therapy for Hemophilia B Prior Authorization Request form (to include physician's order and signature);
2. Clinical documentation supporting the medical necessity of treatment with Hemgenix including the following:
    a. Testing confirming severe or moderately severe factor IX deficiency (≤ 2% of normal circulating factor IX);
    b. Negative factor IX inhibitor test dated within the previous 30 days;
    c. Laboratory testing confirming absence of uncontrolled HIV infection;
    d. Liver health assessments including:
        i. Liver function tests confirming absence of significant liver disease;
        ii. Laboratory testing confirming absence of active hepatitis B virus or hepatitis C virus infection;
        iii. Elastography and/or ultrasound and other laboratory assessments for liver fibrosis; AND
3. Other information as requested.

Requesting Authorization

Requests for the prior authorization of Beqvez or Hemgenix must be submitted by the ordering physician and faxed to the number listed on the request form. Questions regarding this form should be directed to the HUSKY Health Program Utilization Management Department at 1.800.440.5071 (select option for medical authorizations).

Initial Authorization

If approved, authorization will be given for a one-time, single-dose intravenous infusion of Beqvez or Hemgenix.

Reauthorization

Beqvez is indicated as a one-time infusion only. Repeat administration of Beqvez is not supported by FDA labeling or compendia and is therefore not considered medically necessary.

Hemgenix is indicated as a one-time infusion only. Repeat administration of Hemgenix is not supported by FDA labeling or compendia and is therefore not considered medically necessary.

EFFECTIVE DATE

This Policy for the prior authorization of gene therapy for hemophilia B with Beqvez or Hemgenix for individuals covered under the HUSKY Health Program is effective May 1, 2025.

LIMITATIONS
N/A

CODES:

Code	Definition
J1411	Injection, etranacogene dezaparvovec-hyphendrlb, per therapeutic dose
J1414	injection, fidanacogene elaparavovec-dzkt, per therapeutic dose

DEFINITIONS

1. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
2. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
3. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
4. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
5. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
6. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
7. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
8. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested

service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

- Beqvez [package insert]. New York, NY: Pfizer Inc.; Revised April 2024
- Coppens M, Pipe SW, Miesbach W, et al. Etranacogene dezaparvovec gene therapy for haemophilia B (HOPE-B): 24-month post-hoc efficacy and safety data from a single-arm, multicentre, phase 3 trial. *Lancet Haematol*. 2024;11(4):e265-e275. doi:10.1016/S2352-3026(24)00006-1
- Cuker A, Kavakli K, Frenzel L, et al. Gene Therapy with Fidanacogene Elaparvovec in Adults with Hemophilia B. *N Engl J Med*. 2024;391(12):1108-1118. doi:10.1056/NEJMoa2302982
- Hemgenix [package insert]. King of Prussia, PA: CSL Behring LLC.; Revised November 2022
- Malec L. Clinical manifestations and diagnosis of hemophelia A and B. *In:UpToDate*, Shapiro AD and Tirnauer JS (Eds), Wolters Kluwer. Updated December 6, 2024. Accessed January 25, 2025
- U.S. FDA approves Pfizer's Beqvez (fidanacogene elaparvovec-dzkt), a one-time gene therapy for adults with hemophilia B. Press Release. New York, NY: Pfizer; April 26, 2024.

PUBLICATION HISTORY

Status	Date	Action Taken
Original publication	January 2025	Approved at the CHNCT Medical Reviewer meeting on February 12, 2025. Approved by the CHNCT Clinical Quality Subcommittee on March 17, 2025. Approved by DSS on April 3, 2025; 2025