# Drug Coverage Policy

**Effective Date.....06/27/2024**
**Coverage Policy Number.....IP0648**
**Policy Title..... Beqvez**

# Hemophilia – Gene Therapy – Beqvez

- Beqvez™ (fidanacogene elaparvovec-dzkt intravenous infusion - Pfizer)

***INSTRUCTIONS FOR USE***
*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

## Cigna Healthcare Coverage Policy

**OVERVIEW**
Beqvez, an adeno-associated virus (AAV) vector-based gene therapy, is indicated for the treatment of **hemophilia B** (congenital Factor IX deficiency) in adults with moderate to severe disease 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, AND do not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test.[1] The recommended dose of Beqvez is $5 \times 10^{11}$ vector genomes per kg of body weight given as a one-time (per lifetime) single dose as an intravenous infusion. Dose based on adjusted body weight for those with a body mass index > 30 kg/m$^2$.

**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.[2-5] The condition is a rare X-linked bleeding disorder that mainly impacts males. Hemophilia B is four times less common than hemophilia A, which is caused by a relative lack of blood Factor VIII. Approximately 30,000 individuals are living with hemophilia in the US and hemophilia B accounts for around 15% to 20% of hemophilia cases, or around 6,000 patients. Symptoms include heavy or prolonged bleeding following an injury or after a medical procedure. 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. Hemophilia B may be diagnosed when bleeding occurs in infancy or later in life for those with milder disease. There is a strong correlation between Factor IX levels and phenotypic expression of bleeding. Normal plasma levels of Factor IX range from 50% to 150%. 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. Besides gene therapies for the treatment of hemophilia B, Factor IX products, both recombinant and plasma-derived, are used routinely to prevent bleeding or are given on-demand to treat bleeding episodes associated with hemophilia B.

**Clinical Efficacy**

The efficacy of Beqvez was evaluated in one ongoing, prospective, open-label, single-arm, single-dose, multinational, Phase III pivotal trial called BENEGENE-2 involving adult males with moderately severe to severe hemophilia B (Factor IX activity ≤ 2%) [n = 45].[1] All patients completed a prospective lead-in period of at least 6 months in which baseline data were collected while patients were receiving Factor IX products for routine prophylaxis. However, after receipt of Beqvez, use of such products for routine prophylaxis was to be suspended. The trial is ongoing with a planned long-term follow-up of 6 years. Patients were required to be negative for pre-existing neutralizing antibodies to AAVRh74var capsid to participate. Factor IX inhibitors (or a history), uncontrolled human immunodeficiency virus (HIV) infection, or significant liver fibrosis were exclusion criteria. Adequate hepatic and renal function were required. The median follow-up was 2.0 years (range 0.4 to 3.2 years) post-Beqvez administration. The model-derived mean annualized bleeding rate was 4.5 bleeds/year during the baseline lead-in period vs. 2.5 bleeds/year during the post-Beqvez efficacy evaluation period. In total, 60% of patients did not experience any bleeds after receipt of Beqvez; only 29% of patients did not have bleeds in the baseline lead-in period.

## Medical Necessity Criteria

Prior Authorization is recommended for prescription benefit coverage of Beqvez. 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 Beqvez as well as the monitoring required for adverse events and long-term efficacy, approval requires Beqvez 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. 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 Beqvez, 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.

**Documentation:** Documentation is required for use of Beqvez 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.

**Beqvez is considered medically necessary when the following criteria are met:**

**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, O, P, and Q):
   - **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 Beqvez or Hemgenix (etranacogene dezaparvovec-drlb intravenous infusion) is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Beqvez or Hemgenix.
   - **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):
     - **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 does not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid by an approved test **[documentation required]**; AND
   - **G)** Patient meets ALL of the following (i, ii, and iii):
     - **i.** Factor IX inhibitor titer testing has been performed within 30 days **[documentation required]**; AND
     - **ii.** Patient is negative for Factor IX inhibitors **[documentation required]**; AND
     - **iii.** Patient does not have a history of Factor IX inhibitors **[documentation required]**; AND
   - **H)** Prophylactic therapy with Factor IX will not be given after Beqvez administration once adequate Factor IX levels have been achieved; AND
     Note: Use of episodic Factor IX therapy is acceptable for the treatment of bleeds and for surgery/procedures if needed as determined by the hemophilia specialist physician.
   - **I)** 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
   - **J)** According to the prescribing physician, the patient does not have uncontrolled human immunodeficiency virus infection; AND

**K)** Patient has undergone liver function testing within 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 ≤ 1.5 times the upper limit of normal **[documentation required]**; AND
- **iv.** Alkaline phosphatase level is ≤ two times the upper limit of normal **[documentation required]**; AND

**L)** Patient does not have evidence of advanced liver impairment and/or advanced fibrosis; AND
Note: For example, liver elastography (e.g., ≥ 9 kPA) suggestive of or equal to METAVIR Stage 3 disease.

**M)** Within 30 days, the platelet count was ≥ 100 x $10^9$/L **[documentation required]**; AND

**N)** Within 30 days, creatinine was ≤ 2.0 mg/dL **[documentation required]**; AND

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

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

**Q)** If criteria A through P are met, approve one dose (vials in a kit) of Beqvez to provide for a one-time (per lifetime) single dose of 5 x $10^{11}$ vector genomes per kg of body weight by intravenous infusion **[verification required]**. Table 1 provides the number of vials per kit and the National Drug Codes (NDCs) for each kit.
Note: Dose based on adjusted body weight for those with a body mass index > 30 kg/$m^2$ using the following calculation: Dose Weight (kg) = 30 kg/$m^2$ x [Height (m)]$^2$

***** Refer to the Medical Necessity Section Policy Statement.

**Table 1. Beqvez Multi-Vial Kits.[1]**

| Patient Dose Weight | Total Number of Vials per Kit | NDC Number |
|---|---|---|
| ≤ 75 kg | 4 | 0069-2004-04 |
| > 75 to ≤ 95 kg | 5 | 0069-2005-05 |
| > 95 to ≤ 115 kg | 6 | 0069-2006-06 |
| > 115 to ≤ 135 kg | 7 | 0069-2007-07 |

NDC – National Drug Code.

**Dosing.** The recommended dose of Beqvez is a one-time (per lifetime) single dose of 5 x $10^{11}$ vector genomes per kg of body weight by intravenous infusion.
Note: Dose based on adjusted body weight for those with a body mass index > 30 kg/$m^2$ using the following calculation: Dose Weight (kg) = 30 kg/$m^2$ x [Height (m)]$^2$

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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

## Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

| HCPCS Codes | Description |
|---|---|
| C9399 | Unclassified drugs or biologicals |
| J3490 | Unclassified drugs |
| J3590 | Unclassified biologics |

## References


1. Beqvez™ intravenous infusion [prescribing information]. New York, NY: Pfizer; April 2024.
2. 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 May 3, 2024.
3. Sidonio RF, Malec L. Hemophilia (Factor IX deficiency). *Hematol Oncol Clin N Am*. 2021;35:1143-1155.
4. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting factor concentrates to gene editing. *Lancet*. 2021;397:630-640.
5. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin N Am*. 2022;36:797-812.


## Revision Details

| Type of Revision | Summary of Changes | Date |
|---|---|---|
| New | New policy | 06/27/2024 |

The policy effective date is in force until updated or retired.