MEDICAL COVERAGE POLICY	
SERVICE:	**Fidanacogene elaparvovec (Beqvez™)**
Policy Number:	**313**
Effective Date:	**11/01/2024**
Last Review:	**08/12/2024**
Next Review:	**08/12/2025**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

SERVICE: Fidanacogene elaparvovec (Beqvez™)

PRIOR AUTHORIZATION:
POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). Medicare NCD or LCD specific InterQual criteria may be used when available. If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Determination: Baylor Scott & White Health Plan (BSWHP) may consider fidanacogene elaparvovec (Beqvez™) medically necessary for the treatment of members with hemophilia B (congenital factor IX deficiency) when ALL of the following criteria are met.

1. Member is 18 years of age or older **AND**
2. Documentation of moderately severe or severe hemophilia B as evidenced by a baseline (without FIX replacement therapy) FIX level of ≤ 2% of normal **AND**
3. Medication is prescribed by a physician who specializes in hemophilia **AND**
4. Meets one of the following criteria:
    a. Both of the following:
        i. Documentation of receiving routine prophylaxis with FIX therapy continuously for at least 2 months **AND**
        ii. According to the prescriber, has at least a 150-exposure day history of FIX therapy

    OR

    b. Both of the following:
        i. History of life-threatening hemorrhage **AND**
        ii. On-demand use of FIX therapy was required for this life-threatening hemorrhage

    OR

    c. Both of the following:
        i. History of repeated, serious spontaneous bleeding episodes **AND**

ii. On-demand use of FIX therapy was required for these serious spontaneous bleeding episodes

AND

5. Member has adequate liver function as defined by **ONE** of the following:
    a. Both of the following:
        i. Alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase [ALT, AST, or ALP] less than 2 times the upper limit of normal [ULN] **AND**
        ii. Bilirubin less than 1.5 times ULN

    OR

    b. In the presence of sustained liver enzyme elevations, attestation by a consulting hepatologist documenting eligibility to receive sc

    AND

6. Member meets one of the following
    a. Patient is not HIV positive **OR**
    b. Patient is HIV positive and is virally suppressed (< 200 copies of HIV per mL)

    AND

7. Member does **NOT** meet any of the following
    a. Positive test for antibodies to AAVRh74var
    b. FIX inhibitors (i.e. ≥0.6 Bethesda Units [BU])
    c. Active infection with hepatitis B or C virus at screening
    d. Current use of antiviral therapy for Hepatitis B or C
    e. Prior gene therapy

    AND

8. Member must have contraindication or inability to use etranacogene dezaparvovec-drlb (Hemgenix)

BSWHP considers repeat administration of fidanacogene elaparvovec experimental and investigational because the effectiveness of this strategy has not been established.

BSWHP considers fidanacogene elaparvovec to be experimental and investigational for all other indications.

All requests will be reviewed by a clinical pharmacist and medical director.

BACKGROUND:
Hemophilia B is a rare inherited X-linked coagulation disorder. It is caused by mutations in the *F9* gene that prevent adequate production of coagulation factor IX (FIX), a protein essential for blood clot formation. Decreased levels of FIX result in prolonged bleeding that may occur spontaneously or after a traumatic event. The severity of symptoms depends on the degree of FIX deficiency:

Severity	FIX Plasma Levels	Common Symptoms

	(percent of normal)	
Mild	6 - 49 %	Prolonged bleeding usually presenting only after significant trauma or surgery. Diagnosis is often made incidentally.
Moderate	1 - 5 %	Prolonged bleeding usually presenting after trauma, injury, dental work, or surgery. Recurrent joint bleeding may be present in up to 25% of cases. Diagnosis is usually made in late childhood or adulthood.
Severe	< 1 %	Frequent spontaneous bleeding presenting during infancy when disease is most often diagnosed. Bleeding into joints and muscles is common and can lead to intense pain, immobility, and permanent damage if left untreated. Occult bleeding into organs may also occur.

More than 6000 people are living with hemophilia B in the United States. A recent study conducted by the Centers for Disease Control and Prevention (CDC) found that a majority of patients with hemophilia B receive care at a specialized hemophilia treatment center; 70% of the 5106 patients with hemophilia B who received care at a hemophilia treatment center between 2012 and 2018 had moderate or severe disease.

The mainstay of treatment for hemophilia B is replacement of FIX with intravenous infusions of exogenous FIX recombinant or plasma-derived concentrate products. This therapy may be given as needed to treat a bleeding episode (episodic therapy) or routinely to help prevent bleeding episodes and mitigate further damage to joints and organs (prophylactic therapy).

Routine prophylactic therapy to reduce risk for bleeding and ensuing complications is the standard of care for patients with severe or moderate hemophilia B. Prophylaxis is generally effective but has several significant drawbacks. FIX replacement therapy is not a cure. Patients are dependent upon burdensome dosing schedules and monitoring protocols that make adherence to therapy a major challenge. In addition, 3% to 5% of patients with severe hemophilia B develop neutralizing antibodies (inhibitors) to exogenous FIX replacement products. New approaches to the treatment of hemophilia B are needed that address the underlying cause of FIX deficiency and eliminate or reduce dependence on prophylactic therapy. Fidanacogene elaparvovec is an FIX gene transfer product that was developed to address this need.

Gene therapy utilizes a viral vector to carry the desired genetic information to target cells; vectors that are successfully transduced into target cells utilize the cell to express the proteins of interest. The goal of gene therapy is to provide a sustained therapeutic benefit via continual expression of the proteins that modulate the pathogenesis of the relevant disease.

Fidanacogene elaparvovec-dzkt (Beqvez; formerly PF-06838435 and SPK-9001; Pfizer Inc.) is a single-administration, intravenously infused gene therapy for hemophilia B. It combines a viral capsid (adeno-associated virus [AAV]-Spark100) with the gene for factor IX-R338L. Factor IX-R338L, also called FIX-Padua, is a naturally-occurring variant of coagulation factor IX (FIX) that has a high specific activity. The therapeutic viral vector delivers factor IX- R338L DNA to patient cells, where it can be expressed as factor IX-R338L protein. It 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, and do not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test.

It is the second gene transfer therapy for hemophilia B to be approved by the U.S. Food and Drug Administration (FDA). Etranacogene dezaparvovec (Hemgenix; CSL Behring) received FDA approval in November of 2022 and leverages similar technology. These gene transfer therapies will presumably compete with commercially available FIX replacement products indicated for routine prophylactic therapy.

Evidence from the uncontrolled phase III BENEGENE-2 study. Safety and efficacy results of 45 male patients in the BENEGENE-2 study were recently presented at the 68th Annual Meeting of the Society of Thrombosis and Haemostasis Research. The primary endpoint was the annualized bleeding rate for all bleeds occurring between week 12 and month 15 post infusion versus the pre infusion FIX prophylaxis period. The mean annualized bleeding rates were 4.4 during the prophylaxis period and 1.3 at 15 months post infusion (P<0.0001), corresponding to a 71% reduction. The mean annualized bleeding rate was maintained at 0.4 at year 3 in the 21 patients with available data. Sixty-four percent of patients had no bleeding episodes after treatment versus 29% during the prophylaxis period. The annualized FIX infusion rate was 58.8 before treatment and 3.5 after treatment. A total of 6 patients (13%) resumed FIX prophylaxis after treatment with fidanacogene elaparvovec-dzkt (Klamroth et al., 2024).

Published evidence evaluating fidanacogene elaparvovec-dzkt is limited to a report on outcomes from the phase I/II single-arm study, which followed 10 patients with hemophilia B for 1 year after gene therapy with fidanacogene elaparvovec-dzkt (George et al., 2017). Gene therapy was well tolerated and the 10 patients evaluated showed sustained therapeutic expression of the FIX variant (*see* Evidence section).

Long-term safety and efficacy results from 14 participants in a phase I/II study were presented at the 63rd American Society of Hematology (ASH) annual meeting (Samelson-Jones et al., 2021). Follow-up ranged from 2.5 years to > 5 years (n=7 evaluable patients). Three patients had required corticosteroid treatments within the first 6 months after gene therapy. There were no treatment-related serious adverse events. The mean FIX coagulation activity levels were relatively stable over time, ranging from a low of 19.8% of normal (year 5; n=7 evaluable patients) and a high of 25.4% of normal (year 2; n=14 evaluable patients) (Samelson-Jones et al., 2021). The incidence of joint bleeds and other outcomes

within 6 years of gene therapy with fidanacogene elaparvovec-dzkt were presented at the 16th Annual Congress of European Association for Haemophilia and Allied Disorders (Rasko et al., 2023, poster PO163). The mean annualized bleeding rates ranged from 0.1 to 0.9 events per year during follow-up. A total of 3 patients had 6 spontaneous bleeds in joints with known arthropathy during the phase I/II study (i.e., first year following treatment). During long-term follow-up, 3 patients had 17 spontaneous bleeds, most of which were in joints that had spontaneous bleeds during the phase I/II study. During long-term follow-up, 4 patients had a total of 7 traumatic bleeds.

International consensus recommendations from 15 hematology specialists from Europe, Australia, Japan, Latin America, and North America state, "Based on current AAV hemophilia B gene therapy trial data, this therapy should be considered as a future treatment option in adults with severe hemophilia B". This recommendation was published prior to the FDA approval of fidanacogene elaparvovec and publication of pivotal trial results.

A 2020 guideline from the World Federation of Hemophilia (WFH) states, "Gene therapy should make it possible for some people with hemophilia to aspire to and attain much better health outcomes and quality of life than that attainable with currently available hemophilia therapies. This will require evaluation through long-term follow-up as part of clinical trials and registries."

Beqvez has a WAC of $3.5 million and AWP of $4.2 million for a one-time infusion. This is the same listing price that has been set for Hemgenix. Currently, people living with hemophilia B receive IV infusions of FIX that cost approximately $550,000-750,000 annually.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	96365: Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour 96366: Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
HCPCS Codes:	C9399: Unclassified drugs or biologicals *(hospital outpatient use)* J3590: Unclassified biologics
ICD10 codes:	D67: Hereditary factor IX deficiency
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	08/12/2024	New policy

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and make modifications based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Alshaikhli A, Rokkam VR. Hemophilia B. Updated October 9, 2022. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560792/. Accessed March 24, 2023.
2. Buckner TW, Bocharova I, Hagan K, et al. Health care resource utilization and cost burden of hemophilia B in the United States. Blood Adv. 2021;5(7):1954-1962. doi: 10.1182/bloodadvances.2020003424
3. George LA, Sullivan SK, Giermasz A, et al. Hemophilia B gene therapy with a high-specific-activity factor IX variant. N Engl J Med. 017;377(23):2215-2227. doi:10.1056/NEJMoa1708538
4. Hart DP, Matino D, Astermark J, et al. International consensus recommendations on the management of people with haemophilia B. Ther Adv Hematol. 2022;13:20406207221085202. doi:10.1177/20406207221085202
5. Klamroth R, Cuker A, Alzahrani H, et al. Efficacy and safety of fidanacogene elaparvovec in adults with moderately severe or severe hemophilia B: Results from the phase 3 BENEGENE-2 gene therapy trial. Hamostaseologie. 2024;44:S81-S82. doi:10.1055/s-0044-1779185
6. Miller CH. The clinical genetics of hemophilia B (factor IX deficiency). *Appl Clin Genet.* 2021;14:445-454. doi:10.2147/tacg.s288256
7. Perrin GQ, Herzog RW, Markusic DM. Update on clinical gene therapy for hemophilia. *Blood.* 2019;133(5):407-414. doi:10.1182/blood-2018-07-820720
8. Rasko JEJ, Chhabra A, Ducore JM, et al. P0163 Patterns of joint bleeds in patients with hemophilia B following fidanacogene elaparvovec adeno-associated virus gene therapy. *Haemophilia.* 2023;29:113-114. doi:10.1111/hae.14715
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10. Soucie JM, Miller CH, Dupervil B, Le B, Buckner TW. Occurrence rates of haemophilia among males in the United States based on surveillance conducted in specialized haemophilia treatment centres. *Haemophilia.* 2020;26(3):487-493. doi:10.1111/hae.13998
11. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia, 3rd edition. [published correction appears in Haemophilia. July 2021;27(4):699]. *Haemophilia.* 2020;26 Suppl 6:1-158. doi:10.1111/hae.14046
12. Beqvez [package insert]. New York, NY: Pfizer; 2024

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RightCare STAR Medicaid plans are offered through Scott and White Health Plan in the Central Managed Care Service Area (MRSA) and STAR and CHIP plans are offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs.