Oscar Clinical Guideline: Beqvez (fidanacogene elaparvovec) (CG118, Ver. 1)

Beqvez (fidanacogene elaparvovec)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Hemophilia B is a type of bleeding disorder caused by low levels of clotting factor IX (factor IX deficiency), preventing blood from clotting properly. Because factor IX genes are on the X chromosome, severe hemophilia is most common in males because males have only one X chromosome. While females can also get hemophilia, it is usually milder. The severity of hemophilia B is classified based on clotting factor activity level detected in blood and bleeding severity:

- Mild disease:
    - Clotting factor activity level more than 5% but less than 40% of normal (more than 5 but less than 40 units/dL)
    - Frequency of bleeding episodes varies from once a year to once a decade (usually after major trauma)
- Moderate disease:
    - Clotting factor activity level 1% to 5% of normal (1-5 units/dL)

    - Frequency of bleeding episodes varies from one per month to one per year (usually after trauma or minor injury)
- Severe disease:
    - Clotting factor activity level less than 1% of normal (less than 1 unit/dL)
    - Frequent spontaneous bleeding episodes (e.g., 2-5 per month) and after minor injury

Treatment depends on how severe the condition is, and usually involves replacing the missing clotting factor through factor replacement therapy. Factor replacement therapy is given mainly to prevent bleeding or to treat a bleed when it happens.

Beqvez (fidanacogene elaparvovec-dzkt) is an adeno-associated virus (AAV) vector-based gene therapy designed to deliver a functional copy of the FIX gene to liver cells, enabling endogenous production of FIX. Beqvez is administered as a one-time intravenous infusion and is indicated for the treatment of adults with moderate to severe 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.

Definitions

"**Adeno-associated virus (AAV) vector**" refers to a non-pathogenic viral vector used to deliver functional genes to target cells for gene therapy applications.

"**Congenital**" means a condition present from birth.

"**Endogenous**" refers to factors made inside the body.

"**Hemophilia**" is a condition in which blood doesn't clot normally due to missing a protein. There are two main types, hemophilia A (factor VIII is missing or very low) or hemophilia B (factor IX is missing or very low).

"**Hemorrhage**" is the medical term for bleeding.

"**Moderate to severe hemophilia B**" refers to factor IX activity ≤ 2% of normal (< 2 IU/dL), associated with an increased frequency of spontaneous bleeding episodes in joints, muscles, and other tissues/organs.

"**Neutralizing antibodies to AAVRh74var capsid**" refer to pre-existing antibodies against the viral vector capsid serotype used in Beqvez (fidanacogene elaparvovec), which can interfere with successful gene delivery to target cells.

"**Spontaneous**" is to happen without cause or involuntarily.

Medical Necessity Criteria for Authorization

The Plan considers **Beqvez (fidanacogene elaparvovec)** medically necessary when recent (within the last 3 months) clinical chart documentation is provided indicating **ALL** of the following criteria are met:

1. Prescribed by or in consultation with a specialist who has expertise in treating hemophilia B (e.g., hematologist); ***AND***
2. The member meets **ALL** of the following:
    a. is a male 18 years of age or older***; and***
    b. has a diagnosis of congenital hemophilia B and documentation of at least **ONE** of the following:
        i. Severe or moderately severe factor IX deficiency (defined as less than or equal to (≤) 2% of normal circulating endogenous factor IX)***; or***
        ii. Is on continuous routine factor IX prophylaxis***; or***
        iii. Have current or historical life-threatening hemorrhage***; or***
        iv. Have repeated, serious spontaneous bleeding episodes***; AND***
3. The member has no detectable pre-existing neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as demonstrated by a FDA-approved companion diagnostic test (e.g. Labcorp's nAbCyte Anti-AAVRh74var HB-FE assay)[⇅]; ***AND***
    [⇅]*Information on test approved for detection of AAVRh74var preexisting neutralizing antibodies is available at http://www.fda.gov/CompanionDiagnostics.*
4. The member does **NOT** have **ANY** of the following:
    a. Advanced hepatic impairment, including cirrhosis or advanced liver fibrosis (suggestive of or equal to METAVIR Stage 3 disease; e.g., a FibroScan score of ≥9 kPa is considered equivalent)***; or***

b. History of factor IX inhibitors or positive test result for human factor IX inhibitors (i.e., a positive test is ≥0.6 Bethesda units)***; or***
c. Human Immunodeficiency Virus (HIV) infection with a CD4 cell count ≤ 200/mm3 or viral load > 20 copies/mL***; or***
d. Prior treatment with gene therapy for the treatment of hemophilia B***; or***
e. Uncontrolled Hepatitis B or C.

If the above prior authorization criteria are met, the requested product will be authorized for one dose per lifetime, with an approval duration of 6 months.

Medical Necessity Criteria for Reauthorization

There are no medical necessity criteria for reauthorization of Beqvez (fidanacogene elaparvovec-dzkt). It is designed as a single-dose gene therapy product intended to provide durable, potentially lifelong therapeutic benefit following a one-time intravenous infusion. The pivotal BENEGENE-2 trial (NCT03861273) evaluated a single administration of Beqvez (fidanacogene elaparvovec-dzkt) and the FDA-approved prescribing information does not provide any recommendations or evidence supporting repeat doses.

Based on the mechanism of action and available clinical evidence, coverage of Beqvez (fidanacogene elaparvovec-dzkt) is limited to a single one-time infusion per lifetime under the Plan policy. The safety and efficacy of repeat dosing has not been evaluated, and there is no valid rationale or data to support repeat administration at this time. Therefore, reauthorization requests for repeat treatment will be considered not medically necessary.

Experimental or Investigational / Not Medically Necessary

Beqvez (fidanacogene elaparvovec) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Individuals with severe or moderate hemophilia B who do not meet ALL of the required clinical criteria [as outlined in the coverage criteria section, **Medical Necessity Criteria for Authorization**].
- Individuals with mild hemophilia B (factor IX level > 2 IU/dL or > 2% of normal).
- Individuals with a history of or current factor IX inhibitors ≥ 0.6 Bethesda units.

- Individuals with pre-existing neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test.
- Individuals less than 18 years of age.
- Repeat/subsequent administrations of Beqvez following initial one-time infusion.
- Use in combination with other gene therapy products.
- All other indications not outlined under Medical Necessity Criteria for Authorization.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
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)
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
D67	Hereditary factor IX deficiency

References

1. Beqvez (fidanacogene elaparvovec) [prescribing information]. New York, NY: Pfizer Labs; April 2024.
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.
3. Burke T, Asghar S, O'Hara J, et al. Clinical, humanistic, and economic burden of severe hemophilia B in the United States: results from the CHESS US and CHESS US+ population surveys. Orphanet J Rare Dis. 2021;16(1):143.

4. George, L., Sullivan, S., Rasko, J., Giermasz, A., Samelson-Jones, B., Ducore, J., Teitel, J., McGuinn, C., Runowski, A., Wright, F., Anguela, X., High, K., Rybin, D., Murphy, J., & Rupon, J. (2019). Efficacy and Safety in 15 Hemophilia B Patients Treated with the AAV Gene Therapy Vector Fidanacogene Elaparvovec and Followed for at Least 1 Year. Blood. https://doi.org/10.1182/blood-2019-124091.
5. 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
6. 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
7. Mackensen, S., Ducore, J., George, L., Giermasz, A., McGuinn, C., Rasko, J., Samelson-Jones, B., Sullivan, S., Teitel, J., Chhabra, A., Fang, A., O'Brien, A., Plonski, F., Rupon, J., Smith, L., & Winburn, I. (2023). Health-Related Quality of Life in Adults with Hemophilia B after Receiving Gene Therapy with Fidanacogene Elaparvovec. Blood. https://doi.org/10.1182/blood-2023-179431.
8. Miller CH. The clinical genetics of hemophilia B (factor IX deficiency). Appl Clin Genet. 2021;14:445-454. doi:10.2147/tacg.s288256
9. 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
10. 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
11. Samelson-Jones BJ, Sullivan SK, Rasko JEJ, et al. Follow-up of more than 5 years in a cohort of patients with hemophilia B treated with fidanacogene elaparvovec adeno-associated virus gene therapy. Blood. 2021;138:3975. doi:10.1182/blood-2021-150541
12. 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
13. World Federation of Hemophilia. Report on the annual global survey 2021. October 2022. Available at: https://www1.wfh.org/publications/files/pdf-2324.pdf

Clinical Guideline Revision / History Information

Original Date: 06/27/2024
Reviewed/Revised: