Beqvez™ (fidanacogene elaparvovec-dzkt)
(Intravenous)

Effective Date: 11/1/2024
Review Date:8/14/2024
Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

I. Length of Authorization

Coverage will be provided for one dose and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 1 kit (based on weight chart below)

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1 kit (based on weight chart below)

III. Summary of Evidence

Beqvez is a one-time gene therapy for the treatment of moderate to severe hemophilia B. The approved indication includes adults who currently use factor IX (FIX) prophylaxis therapy, have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes, and do not have neutralizing antibodies to adeno-associated virus (AAV) serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test. Beqvez acts as an AAV-based gene therapy designed to introduce a functional copy of the FIX gene into the transduced cell, where it will then encode a high-activity FIX variant. Beqvez is administered as a one-time single-dose IV infusion only. FDA approval is based on results from the pivotal Phase 3 BENEGENE-2 study, an open-label, single-arm study that enrolled 45 adult males with moderately severe to severe hemophilia B who completed a minimum of 6 months of routine FIX prophylaxis therapy during the lead-in study. Patients received a single intravenous (IV) infusion of Beqvez at a dose of 5 × 10^11 vector genomes per kilogram (vg/kg) of body weight. The trial demonstrated noninferiority in annualized bleeding rates (ABRs) compared with standard-of-care (SOC) FIX therapy. Treatment with Beqvez resulted in a mean ABR of 2.5 in the efficacy evaluation period between Week 12 and data cutoff (median 1.8 years of follow-up), compared to a mean ABR of 4.5 during the lead-in pretreatment period of at least 6 months (median 1.2 years of follow-up). Bleeds were eliminated in 60% of patients compared to 29% in the SOC prophylaxis arm. The data showed that Beqvez was

generally well tolerated, with the most common adverse event being elevated transaminases. No serious adverse events or deaths have been reported.

IV. Initial Approval Criteria [1-11]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable.

Coverage is provided in the following conditions:

Hemophilia B (Congenital Factor IX Deficiency) †

- Patient is at least 18 years of age; **AND**
- Beqvez must be prescribed by, or consultation with a hematologist; **AND**
- Patient will undergo treatment at a manufacturer approved Qualified Treatment Center (QTC); **AND**
- Patient has a diagnosis of moderately severe or severe congenital factor IX deficiency (i.e., ≤2% of normal circulating factor IX), as confirmed by blood coagulation testing, for which the subject is on continuous routine factor IX prophylaxis, unless there is a contraindication or intolerance*(Note: Continuous routine prophylaxis is defined as the intent of treating with an a priori defined frequency of infusions (e.g., twice weekly, once every two weeks, etc.) as documented in the medical records)*; **AND**
- Patient has not received prior hemophilia AAV-vector–based gene therapy (e.g., Hemgenix [etranacogene dezaparvovec]); **AND**
- Patient has one or more of the following:
    - Currently use Factor IX prophylaxis therapy (e.g., AlphaNine SD, Alprolix, BeneFIX, Idelvion, Ixinity, Mononine, Profilnine, Rebinyn, Rixubis, etc.); **OR**
    - Have current or historical life-threatening hemorrhage; **OR**
    - Have repeated, serious spontaneous bleeding episodes, *(e.g., intramuscular hematomas requiring hospitalization, hemarthrosis, central nervous system (CNS) bleeding (including intracranial hemorrhage), pulmonary hemorrhage, life-threatening gastrointestinal (GI) hemorrhage and umbilical cord bleeding)*; **AND**

- Patient has been tested and found negative for Factor IX inhibitor titers (i.e., <0.6 Bethesda Units) and does not have a prior history of inhibitors *(Note: if test result is positive, re-test within approximately 2 weeks. If re-test is also positive, Beqvez (fidanacogene elaparvovec) should not be given)*; **AND**
- Patient Factor IX activity will be monitored periodically (e.g., weekly for 3 months) as well as presence of inhibitors if bleeding is not controlled (*Note: patients will continue to require exogenous Factor IX until response to Beqvez (fidanacogene elaparvovec) occurs*); **AND**
- Patient will discontinue Factor IX prophylaxis therapy upon achieving FIX levels of 5% from Beqvez (fidanacogene elaparvovec) treatment; **AND**
- Patient is adeno-associated virus serotype Rh74var capsid (AAVRh74var) neutralizing antibody negative as determined by an FDA-approved or CLIA-compliant test**; **AND**
- Patient will have baseline liver function assessed prior to and after therapy according to the monitoring schedule outlined in the product labeling with corticosteroids administered in response to elevations; **AND**
- Patients with preexisting risk factors for hepatocellular carcinoma (e.g., patients with cirrhosis, advanced hepatic fibrosis, hepatitis C or B, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption, non-alcoholic steatohepatitis (NASH), and advanced age) will have abdominal ultrasound screenings and be monitored regularly (e.g., annually) for alpha-fetoprotein (AFP) elevations following administration; **AND**
- Patient does not have current liver-related coagulopathy, hypoalbuminemia, persistent jaundice, or cirrhosis), portal hypertension, splenomegaly, hepatic encephalopathy, hepatic fibrosis, or active viral hepatitis; **AND**
- Patient has been tested for HIV and does not have an active infection (i.e., either CD4+ cell count <200 mm^3 or viral load ≥20 copies/mL in cases of serological evidence of HIV-1 or HIV-2 infection)**; AND**
- Patient has been counseled on avoidance of potentially hepatoxic substances (e.g., alcohol) which may reduce the efficacy of Beqvez (fidanacogene elaparvovec)

Notes:

- Monitor Factor IX activity levels as outlined in the prescribing information to confirm adequate endogenous Factor IX activity levels to support discontinuation of pre-infusion Factor IX prophylaxis therapy.
- Exogenous Factor IX or other hemostatic products may also be required in case of surgery, invasive procedures, trauma, or bleeds in the event that fidanacogene elaparvovec-derived Factor IX activity is deemed insufficient for adequate hemostasis in such situations.
- Use of exogenous Factor IX concentrates before and after fidanacogene elaparvovec administration may impede assessment of endogenous, fidanacogene elaparvovec-derived Factor IX activity.

**If confirmed using an immunotherapy assay-*http://www.fda.gov/companiondiagnostics*

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); **Φ** Orphan Drug

V. Renewal Criteria

Coverage cannot be renewed.

VI. Dosage/Administration

Indication	Dose
Hemophilia B (Congenital Factor IX Deficiency	The recommended dose of Beqvez is a single-dose intravenous infusion of 5×10^{11} vector genomes per kg (vg/kg) of body weight. **Calculate patient's dose weight:** – Dosing is based on the patient's body mass index (BMI) in kg/m^2

Patient's BMI	Patient's Dose WEight
≤ 30 kg/m^2	Dose Weight=Actual body weight

	>30 kg/m^2	Determine using the following calculation: Dose Weight (kg) = 30 kg/m^2 x [Height (m)]^2

<u>Calculation of patient's dose volume in mL</u>:

– Dose weight in kilograms (kg) divided by 20 = dose in mL
(The division factor 20 represents the amount of vector genomes per mL of the Beqvez suspension (1×10^{13} vg/mL) divided by the per kilogram dose (5×10^{11} vg/kg))

- *Beqvez contains genetically modified vectors. Personal protective equipment (including gloves, safety goggles, laboratory coat and sleeves) should be worn while preparing or administering.*
- *Confirm that the patient's identity matches the patient-specific identifier number on the outer carton.*
- *Store in the original package to avoid direct sunlight and ultraviolet light exposure.*
- *Thaw Beqvez vials for 1 hour at room temperature 15 °C to 30 °C (59 °F to 86 °F) in the upright orientation in the inner carton. Vials may be gently swirled but not shaken or inverted.*
- *DO NOT administer as an intravenous push or bolus.*
- *DO NOT infuse the diluted suspension in the same intravenous line with any other products.*
- *DO NOT use a central line or port.*

VII. Billing Code/Availability Information

<u>HCPCS code:</u>

- C9172 – Injection, fidanacogene elaparvovec-dzkt, per therapeutic dose*(Effective 10/1/2024)*

<u>NDC:</u>

Beqvez Multi-Vial kit sizes:

Patient Dose Weight (kg)	Total number of vials per Kit	NDC
≤75	4	00069-2004-04
>75 to ≤95	5	00069-2005-05
>95 to ≤115	6	00069-2006-06
>115 to ≤135	7	00069-2007-07

MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

VIII. References

1. Beqvez [package insert]. New York, NY; Pfizer, Inc., April 2024. Accessed April 2024.
2. MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Selected Disorders of the Coagulation System. National Hemophilia Foundation. MASAC Document #284; April 2024. Available at: https://www.bleeding.org/healthcare- professionals/guidelines-on-care/masac-documents/masac-document-284-masac- recommendations-concerning-products-licensed-for-the-treatment-of-hemophilia-and- selected-disorders-of-the-coagulation-system. Accessed May 2024.
3. Guidelines for the Management of Hemophilia. 3rd Edition. World Federation of Hemophilia 2020. Available at: https://www1.wfh.org/publications/files/pdf-1863.pdf. Accessed May 2024.
4. Graham A1, Jaworski K. Pharmacokinetic analysis of anti-hemophilic factor in the obese patient. Haemophilia. 2014 Mar;20(2):226-9.
5. Croteau SE1, Neufeld EJ. Transition considerations for extended half-life factor products. Haemophilia. 2015 May;21(3):285-8.
6. Mingot-Castellano, et al. Application of Pharmacokinetics Programs in Optimization of Haemostatic Treatment in Severe Hemophilia a Patients: Changes in Consumption, Clinical Outcomes and Quality of Life. Blood. 2014 December; 124 (21).
7. MASAC RECOMMENDATION CONCERNING PROPHYLAXIS FOR HEMOPHILIA A AND B WITH AND WITHOUT INHIBITORS. National Hemophilia Foundation. MASAC Document #267 (Replaces Document #241); March 2022. Available at: https://www.bleeding.org/sites/default/files/document/files/267_Prophylaxis.pdf. Accessed May 2024.
8. Rayment R, Chalmers E, Forsyth K, et al. Guidelines on the use of prophylactic factor replacement for children and adults with Haemophilia A and B. B J Haem:190;5, Sep 2020. https://doi.org/10.1111/bjh.16704.
9. Peyvandi F, Palla R, Menegatti M, et al. Coagulation factor activity and clinical bleeding severity in rare bleeding disorders: results from the European Network of Rare Bleeding Disorders. *J Thromb Haemost.* 2012;10:615-621.
10. Thornburg, C.D., Simmons, D.H., von Drygalski, A. Evaluating gene therapy as a potential paradigm shift in treating severe hemophilia. BioDrugs. 2023. DOI: 10.1007/s40259-023- 00615-4.
11. 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(S 01): S81-S82. DOI: 10.1055/s-0044-1779185.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D67	Hereditary factor IX deficiency

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self- administered. The following link may be used to search for NCD, LCD, or LCA documents https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC

M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Beqvez was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Beqvez according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.