09-J4000-92

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Reviewed: 08/14/24

Revised: 01/01/25

Subject: Fidanacogene Elaparvovec (Beqvez)

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DESCRIPTION:

Fidanacogene elaparvovec (Beqvez), an adeno-associated virus (AAV) vector–based gene therapy, was approved by the U.S. Food and Drug Administration (FDA) in 2024 for the treatment of adults with moderate to severe Hemophilia B (congenital Factor IX deficiency) who currently use Factor IX 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 serotype Rh74var (AAVRh74var) capsid. This is the second FDA-approved gene therapy for this indication. Fidanacogene elaparvovec is a one-time intravenous infusion, which delivers a functional copy of the human Factor IX (hFIX) gene into target liver cells, enabling patients to endogenously synthesize their own therapeutic FIX protein.

The safety and efficacy of fidanacogene elaparvovec were evaluated in an open-label, single arm study of adult males with moderately severe to severe hemophilia B and FIX levels of less than or equal to 2% of normal (BeneGene-2, NCT03861273). Subjects were required to have received prophylaxis therapy for a minimum of six months with at least 50 documented exposure days to a factor IX product. Patients with a history of FIX inhibitors, active infection with hepatitis B or C, or prior gene therapy were excluded. All subjects received a single intravenous dose of fidanacogene elaparvovec at a dose of 5 × 1011 vg/kg and entered a follow-up period of 6 years. (n=45). Of the 45 patients, 41 completed at least 15 months of FU. The median follow-up of the 45 treated patients was 2.0 years (range: 0.4 to 3.2 years) from the time of infusion. The primary efficacy outcome for the analysis was a non-inferiority evaluation of the difference in ABR during the post-treatment evaluation period compared with baseline.

The following table summarizes the noninferiority comparison between the mean ABR after fidanacogene elaparvovec therapy and the mean baseline ABR while patients were on factor IX prophylaxis.

ABR and Bleeding Events	Baseline	Post-Fidanacogene Elaparvovec Efficacy Evaluation Period
Median (range) of follow-up time (years)	1.2 (0.6, 2.4)	1.8 (0.2, 3.0)
Total follow-up time (person-years)	59	83
Median (min, max) ABR (bleeds/year)[‡]	1.3 (0.0, 53.9)[‡]	0.0 (0.0, 19.0)
Model derived mean ABR [bleeds/year] (95% CI)[†§]	4.5 (1.9, 7.2)	2.5 (1.0, 3.9)
n (%) of patients without any bleeds	13 (29%)	27 (60%)
Total number of observed bleeds	225	98
Number of observed spontaneous bleeds (proportion of total bleeds)	157 (70%)	60 (61%)
Number of observed joint bleeds (proportion of total bleeds)	184 (82%)	71 (72%)

ABR = Annualized Bleeding Rate for all bleeds (treated and untreated with factor IX, excluding procedural bleeds).

CI = confidence interval.

*Post-BEQVEZ efficacy evaluation period is from Week 12 (Day 82) to data cutoff.

†A total of 7 participants (16%) had used factor IX replacement products during the efficacy evaluation period for extended prophylaxis that confounded the treatment effect of BEQVEZ, with a median start time at 0.8 (range: 0.4 to 1.1) years. An ABR of 20 bleeds/year was imputed for the confounded periods.

‡The results presented in this table included data on a participant with a baseline ABR of 53.9 bleeds/year, which disproportionately influenced the baseline ABR estimate. A post-hoc sensitivity analysis, excluding this participant, still met the non-inferiority study success criterion.

§Model-based ABR estimates from a repeated measures generalized linear model with negative binomial distribution and identity link function.

The model derived mean ABR was 4.5 bleeds/year (95% CI: 1.9, 7.2) during the baseline period and 2.5 bleeds/year (95% CI: 1.0, 3.9) post-infusion, resulting in a difference between the mean post-infusion ABR and the baseline ABR of -2.1 bleeds/year (95% CI: -4.8, 0.7). The upper bound of the 95% CI in the difference was less than 3.0 bleeds/year, meeting the non-inferiority study success criterion. Six out of 45 patients (13%) resumed routine factor IX prophylaxis after treatment, starting from 0.4 years to 1.7 years after infusion. An additional patient had intermittent exogenous factor IX use and had a higher ABR post infusion (5.0 bleeds/year) compared to baseline (1.2 bleeds/year) with a factor IX activity <5% (SynthASil assay) starting at 0.4 years. The most common adverse reaction occurring in 5% or more of patients was an increase in transaminases.

POSITION STATEMENT:

Fidanacogene elaparvovec (Beqvez) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with hemophilia B

2. Member's endogenous factor IX is less than or equal to 2 IU/dL (2%) – laboratory documentation must be provided
3. Member has been seen by a board-certified hematologist-oncologist or hematologist in the past 12 months – documentation from medical record must be provided, including ALL of the following:
    a. Complete hematologic and musculoskeletal assessment
    b. Factor replacement protocol (including dosing for both acute and prophylactic management)
    c. Treatment log documenting any bleeds and required treatment within the past 12 months
4. Member does not have inhibitors to factor IX
5. Member does not have antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) – laboratory documentation must be provided
6. The member does NOT have significant liver dysfunction as defined by abnormal elevation of any of the following – laboratory documentation within the past 3 months must be provided:
    a. ALT (alanine transaminase) 3 times the upper limit of normal
    b. Bilirubin above 3 times the upper limit of normal
    c. Alkaline phosphatase above 3 times the upper limit of normal
    d. INR (international normalized ratio) greater than or equal to 1.4
7. Member has had clinically evident bleeding (defined as: 1 or more episodes of spontaneous bleeding into a joint or into the central nervous system; or 4 or more episodes of soft tissue bleeding in an 8-week period) after a two-month trial of at least one factor IX prophylaxis regimen – documentation from the medical record must be provided
8. Member was previously approved by Florida Blue for a factor IX prophylaxis regimen
9. Member does not have a history of prior gene therapy use (including prior treatment with etranacogene dezaparvovec [Hemgenix] or fidanacogene elaparvovec [Beqvez])
10. Fidanacogene elaparvovec is prescribed by a board-certified hematologist or hematologist-oncologist
11. Dose does not exceed 5 x 10^{11} vector genomes per kilogram (vg/kg)
12. If member has a BMI greater than 30 kg/m^2, dose is based on adjusted body weight – documentation from the medical record must be provided
13. Member is at least 18 years of age

Approval duration: 6 months (1 lifetime treatment)

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- For one-time single-dose intravenous infusion only
- Perform baseline testing to select patients, including testing for pre-existing antibodies to AAVRh74var, factor IX inhibitor presence, and liver health tests
- The recommended dose is 5 × 1011 vector genomes per kg (vg/kg) of body weight. Dose based on adjusted body weight for those with a BMI >30 kg/m2
- Administer as an intravenous infusion after dilution in 0.9% sodium chloride with 0.25% human serum albumin (HSA) with a final volume of 200 mL over approximately 60 minutes

Dose Adjustments

- None

Drug Availability

- Suspension for intravenous infusion after dilution
- Nominal concentration of 1 × 1013 vg/mL, and each vial contains an extractable volume of 1 mL
- The total number of vials will be customized to meet dosing requirements for individual patients based on their weight

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Hepatotoxicity: Monitor transaminases and factor IX activity levels once or twice weekly for at least 4 months after BEQVEZ administration to mitigate the risk of potential hepatotoxicity. Consider corticosteroid treatment for transaminase elevation or a decline in factor IX activity.
- Infusion Reactions: Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or stop administration. Restart infusion at a slower rate once reaction has resolved.
- Malignancy: Monitor patients with risk factors for hepatocellular carcinoma (e.g., hepatitis B or C, non-alcoholic fatty liver disease, chronic alcohol consumption, non-alcoholic steatohepatitis, advanced age) with regular liver ultrasound (e.g., annually) and alpha-fetoprotein testing for 5 years following administration. In the event that a malignancy occurs after treatment with BEQVEZ, contact Pfizer Inc. at 1-800-438-1985.

BILLING/CODING INFORMATION:

HCPCS Coding

J1414	Injection, fidanacogene elaparvovec-dzkt, per therapeutic dose

ICD-10 Diagnosis Codes That Support Medical Necessity

D67	Hereditary factor IX deficiency

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

Clotting Factors and Coagulant Drug Products, 09-J0000-34
Etranacogene Dezaparvovec (Hemgenix), 09-J4000-44

OTHER:

None

REFERENCES:

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2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 07/30/24]. Available from: http://www.clinicalpharmacology.com/.
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6. Pfizer. Beqvez (fidanacogene elaparvovec-dzkt) kit. 2024 [cited 8/2/24]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5f477a47-bdc2-41fb-a720-30f9809dc6e8

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 08/14/24.

GUIDELINE UPDATE INFORMATION:

09/15/24	New Medical Coverage Guideline.
10/01/24	Revision: Added HCPCS code C9172.
01/01/25	Revision: Added HCPCS code J1414 and deleted codes C9172 and J3590.