Pharmacy Focus:
Hemgenix® and Beqvez™ — Gene Therapies for Hemophilia B

Key Takeaways

- Hemgenix (approved November 22, 2022) and Beqvez (approved April 26, 2024) are indicated for adults with Hemophilia B (without inhibitors) who use prophylactic treatment and have a history of life-threatening bleeds or repeated serious spontaneous bleeding episodes.
- These one-time therapies were created to potentially increase Factor IX levels to reduce both bleeding episodes and the need for prophylactic therapy.
- Both therapies are priced at $3,500,000 for a one-time dose.

Hemophilia B Disease Overview[1,2,3,4,5]

Hemophilia is a rare disorder characterized by excessive bleeding due to impaired blood clotting, most commonly presenting with unusual bruising and bleeding, which can be both external or internal. Excessive bleeding can occur with cuts or scrapes, dental work and surgeries. However, with more severe cases, bleeds can appear spontaneously. Larger joints, such as knees, ankles and elbows, are most commonly affected.

There are different types of hemophilia including Hemophilia A, Hemophilia B, and von Willebrand Disease (only Hemophilia B will be covered in this focus). Hemophilia B (or Christmas Disease) is caused by decreased or absent levels of clotting Factor IX. Patients with Hemophilia B may have mild, moderate or severe disease based on their Factor IX levels.

Hemophilia B more commonly affects males than females, with all races and ethnic groups affected equally. It is estimated that about 6,000 males in the United States have Hemophilia B. Generally, those with severe disease will be diagnosed between birth and the first few years of life, while those with mild or moderate cases or acquired hemophilia may not be diagnosed until later in life.

Current Treatment Options[5]

The current standard of care treatment for those with Hemophilia B is the replacement of Factor IX clotting factors to prevent bleeding episodes and other complications. Factor replacement products can be derived from human blood/plasma or be recombinant (manufactured in a laboratory with no human blood proteins). Recombinant factor replacement products are favored, as they have no risk of virus transmission.

Complications of factor replacement therapy can include infusion reactions and the development of inhibitors. Inhibitors prevent the current factor treatments from working the same as before, making it more difficult to prevent or stop a bleeding episode. The presence of inhibitors requires the use of increased doses and can end up costing more than $1.5 million per year, versus $500,000 to $1,100,000 for severe patients without inhibitors.

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There are now two gene therapies approved for treatment of severe Hemophilia B — Hemgenix and Beqvez. Both gene therapies are designed to deliver a function copy of the gene that helps to increase Factor IX activity using an adeno-associated virus vector (AAV5). Both have a price tag of $3,500,000 for a one-time infusion.

	Factor IX Replacement Products (e.g., Alprolix®, Idelvion®, Rixubis®, etc.)	**Hemgenix®**	**Beqvez™**
FDA Approved Use	**For children and adults who need:** • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis	**For adults who:** • Currently use Factor IX prophylaxis • Have any history of life-threatening bleeds • Have a history of repeated, serious bleeding episodes	**For adults who:** • Currently use Factor IX prophylaxis • Have any history of life-threatening bleeds • Have a history of repeated, serious bleeding episodes
Average Annual Cost	$500,000 to $1,100,000*	$3,500,000 for a one-time infusion plus up to six months of continued prophylaxis following Hemgenix	$3,500,000 for a one-time infusion plus up to six months of continued prophylaxis following Beqvez
Payment Structures	Medical and/or Prescription Benefits	Medical Benefits	Medical Benefits
HCPCS Codes for Medical Billing	J7193-J7195, J7200-J7202	J1411	J3490, J3590, C9399

**Average cost for Factor IX replacement products seen in HM Insurance Group cases (2021-2023).*

Hemgenix and Beqvez Overview[6,7]

Hemgenix, produced by CSL Behring, was approved November 22, 2022, and Beqvez, produced by Pfizer, was approved April 24, 2024. Both are approved for use in adult patients with Hemophilia B who currently use Factor IX prophylaxis, have had a life-threatening bleed or have had repeated, serious, spontaneous bleeding episodes. There is a low likelihood of use in patients with comorbidities including HIV, hepatitis, end organ disease and thromboembolic events. Patients who currently have inhibitors present and liver abnormalities/disease are not eligible to receive Hemgenix or Beqvez. Neither of the gene therapies were studied in women, pediatric patients younger than 18 or geriatric patients older than 65 years.

Overall, the goal of the one-time gene therapies is to increase the production of Factor IX clotting factor to reduce both bleeding episodes and the need for prophylactic and/or as-needed factor replacement therapy. The full effect of either therapy can take weeks to months. Participants in the clinical trial for Hemgenix continued prophylactic treatment for at least six months after receiving the gene therapy infusion, with two of 54 participants unable to stop at all. After receiving Hemgenix or Beqvez, most participants attained Factor IX levels similar to that of those with mild disease severity, requiring only as-needed Factor IX replacement treatment for acute bleeding episodes. In the BENEGENE-2 trial for Beqvez, bleeds were eliminated in 60% of patients compared to 29% in the prophylaxis arm, and the annualized bleed rate (ABR) median was reduced (median of zero in the treatment arm versus 1.3 in the prophylaxis arm). The durability of either treatment remains to be seen, but participants have been studied for at least 24 months for Hemgenix and six years for Beqvez.

Cost Containment Considerations

As part of its HMConnects™ cost containment program, HM Insurance Group (HM) works to support cost management opportunities around the use of gene and cell therapies and other high-cost pharmaceutical treatment options that can impact our clients' bottom line. The Pharmacy Operations (RxOps) team watches the market — and our book of business — to anticipate how current and future advancements will impact financial risk levels for HM's client base. Standard practices include reviewing, auditing and collaborating on the content of current policies, monitoring trends and implementing appropriate cost savings techniques. Additional practices include identifying the stockpiling of medications, determining if prescriptions are filled via in-network pharmacies and confirming that prescriptions are properly dosed based on weight and lab values when appropriate. All of these services are provided to HM's clients at no additional cost to them.

Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

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Resources: [1]"Hemophilia," Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/hemophilia/symptoms-causes/syc-20373327, accessed April 4, 2024; [2]"Treatment of Hemophilia," CDC, https://www.cdc.gov/ncbddd/hemophilia/data.html, accessed April 4, 2024; [3]"Data & Statistics on Hemophilia," CDC, https://www.cdc.gov/ncbddd/hemophilia/data.html, accessed April 4, 2024; [4]"Hemophilia B," GARD, https://rarediseases.info.nih.gov/diseases/8732/hemophilia-b, accessed April 4, 2024; [5]"Hemophilia B," National Hemophilia Foundation, https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b, accessed April 26, 2024; [6]Hemgenix, package insert, CSL Behring LLC, 2022; [7]Phase III, Open-label, Single-dose, Multi-center, Multinational Trial Investigating a Serotype 5 Adeno-associated Viral Vector Containing the Padua Variant of a Codon-optimized Human Factor IX Gene (AAV5-hFIXco-Padua, AMT-061) Administered to Adult Subjects With Severe or Moderately Severe Hemophilia B, ClinicalTrials.gov identifier: NCT03569891, https://clinicaltrials.gov/ct2/show/NCT03569891, accessed November 23, 2022; [8]Beqvez, package insert, Pfizer, 2024; [9]"U.S. FDA Approves Pfizer's BEQVEZ™ (fidanacogene elaparvovec-dzkt), a One-Time Gene Therapy for Adults with Hemophilia B," businesswire, https://www.businesswire.com/news/home/20240425269649/en/U.S.-FDA-Approves-Pfizer's-BEQVEZ™-fidanacogene-elaparvovec-dzkt-a-One-Time-Gene-Therapy-for-Adults-with-Hemophilia-B, accessed April 26, 2024; [10]A Study to Evaluate the Efficacy and Safety of Factor IX Gene Therapy with PF-06838435 in Adult Males with Moderately Severe to Severe Hemophilia B (BENEGENE-2), ClinicalTrials.gov identifier: NCT03861273, https://clinicaltrials.gov/study/NCT03861273 , accessed April 26, 2024.

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