Optum Rx®

Hemgenix® (etranacogene dezaparvovec-drlb) – New orphan drug approval

- On November 22, 2022, the FDA announced the approval of CSL Behring's Hemgenix (etranacogene dezaparvovec-drlb), for 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.

- Hemophilia B is a genetic bleeding disorder resulting from missing or insufficient levels of blood clotting Factor IX. Most individuals who have Hemophilia B and experience symptoms are men. The prevalence of Hemophilia B in the population is about one in 40,000; Hemophilia B represents about 15% of patients with hemophilia.
    - Treatment typically involves replacing the missing or deficient clotting factor to improve the body's ability to stop bleeding and promote healing. Patients with severe Hemophilia B typically require a routine treatment regimen of intravenous (IV) infusions of Factor IX replacement products to maintain sufficient levels of clotting factor to prevent bleeding episodes.

- Hemgenix is a one-time gene therapy product given as a single dose by IV infusion. Hemgenix consists of a viral vector carrying a gene for clotting Factor IX. The gene is expressed in the liver to produce Factor IX protein, to increase blood levels of Factor IX and thereby limit bleeding episodes.

- The efficacy of Hemgenix was established in an open-label, single-arm study in 54 adult male patients aged 19 to 75 years, with severe or moderately severe Hemophilia B. Patients prospectively completed a lead-in period of at least 6 months with the intent to receive standard of care routine Factor IX prophylaxis. Patients then received a single IV dose of Hemgenix. The main efficacy outcome was a non-inferiority test of annualized bleeding rate (ABR) during months 7 to 18 after Hemgenix treatment compared with ABR during the lead-in period.
    - The estimated mean ABR during months 7 to 18 after Hemgenix treatment was 1.9 bleeds/year (95% CI: 1.0, 3.4), compared with an estimated mean ABR of 4.1 bleeds/year (95% CI: 3.2, 5.4) during the lead-in period.
    - The ABR ratio (months 7 to 18 post-treatment / lead-in) was 0.46 (95% CI: 0.26, 0.81), demonstrating non-inferiority of ABR during months 7 to 18 compared to the lead-in period.
    - Two patients were not able to stop routine prophylaxis after Hemgenix treatment. During months 7 to 18, an additional patients received prophylaxis from days 396 to 534.

- Warnings and precautions for Hemgenix include infusion reactions, hepatotoxicity, immune-mediated neutralization of the AAV5 vector capsid, hepatocellular carcinogenicity, and monitoring laboratory tests.

- The most common adverse reactions (≥ 5%) with Hemgenix use were elevated alanine aminotransferase, headache, blood creatine kinase elevations, flu-like symptoms, infusion-related reactions, fatigue, malaise, and elevated aspartate aminotransferase.

- The recommended dose of Hemgenix is 2 x 10^{13} genome copies (gc) per kilogram (kg) of body weight (or 2 mL/kg body weight) administered as an intravenous infusion after dilution with 0.9% sodium chloride solution.

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  - Refer to the Hemgenix drug label for complete dosing and administration recommendations.
  - Hemgenix can be administered only once.

- Hemgenix will be priced at $3.5 million for a one-time dose.

- CSL Behring plans to launch Hemgenix as soon as possible. Hemgenix will be available in kits containing 10 to 48 single-use vials, each kit constituting a dosage unit based on the patient's body weight. Hemgenix has a nominal concentration of 1×10^{13} gc/mL, and each vial contains an extractable volume of not less than 10 mL.