Roctavian™ (valoctocogene roxaparvovec-rvox) – New orphan drug approval

- On June 29, 2023, BioMarin announced the FDA approval of Roctavian (valoctocogene roxaparvovec-rvox), for the treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) without antibodies to adeno-associated virus serotype 5 (AAV5) detected by an FDA-approved test.

- Hemophilia A is a blood disorder caused by a mutation in the gene responsible for producing a protein called factor VIII, which is necessary for blood clotting. Patients with severe hemophilia A are at risk for painful and potentially life-threatening bleeds, which can occur spontaneously.

    - Approximately 1 in 10,000 people have hemophilia A and about 50% of patients with the condition have severe disease.
    - BioMarin expects approximately 2,500 adults in the U.S. to be eligible to receive Roctavian.

- Roctavian is the first gene therapy approved for hemophilia A. Roctavian works by delivering a functional gene that is designed to enable the body to produce factor VIII on its own, reducing the need for ongoing prophylaxis.

- The efficacy of Roctavian was established in an open-label, single-dose, single-arm study in 134 adult males (18 years of age and older) with severe hemophilia A, who received a single intravenous (IV) dose of Roctavian. Of the 134 patients who received Roctavian, 112 patients had baseline annualized bleeding rate (ABR) data prospectively collected during a period of at least six months on factor VIII prophylaxis prior to receiving Roctavian (rollover population). The primary outcome was a non-inferiority (NI) test of the difference in ABR in the efficacy evaluation period (EEP) following Roctavian administration compared with ABR during the baseline period in the rollover population.

    - The mean EEP ABR was 2.6 bleeds/year, compared to a mean baseline ABR of 5.4 bleeds/year. The mean difference in ABR was -2.8 (95% CI: -4.3, -1.2) bleeds/year. The NI analysis met the pre-specified NI margin.

- Roctavian is contraindicated in patients with:

    - Active infections, either acute (such as acute respiratory infections or acute hepatitis) or uncontrolled chronic (such as chronic active hepatitis B)
    - Known significant hepatic fibrosis or cirrhosis
    - Patients with known hypersensitivity to mannitol.

- Warnings and precautions for Roctavian include infusion-related reactions; hepatotoxicity; thromboembolic events; monitoring laboratory tests; and malignancy.

- The most common adverse reactions (≥ 5%) with Roctavian use were nausea, fatigue, headache, infusion-related reactions, vomiting, and abdominal pain. The most common laboratory abnormalities (≥ 10%) were alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatine phosphokinase, factor VIII activity levels, gamma-glutamyl transferase and bilirubin > upper limit of normal.

- The recommended dose of Roctavian is 6×10^{13} vector genomes per kilogram (vg/kg) body weight, administered as a single IV infusion.

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  - Testing for pre-existing antibodies to AAV5 should be performed using the FDA approved companion diagnostic. Roctavian should not be administered to patients with a positive test for antibodies to AAV5. Information on FDA-approved tests for the detection of antibodies to AAV5 is available at: http://www.fda.gov/CompanionDiagnostics.
  - Refer to the Roctavian drug label for complete dosing and administration recommendations.

- The wholesale acquisition cost (WAC) for Roctavian will be $2.9 million for a one-time dose.

- BioMarin launch plans for Roctavian are pending. Roctavian will be available as a 2×10^{13} vg/mL suspension for intravenous infusion.