## Hympavzi™ (marstacimab-hncq) – New orphan drug approval

- On October 11, 2024, Pfizer announced the FDA approval of Hympavzi (marstacimab-hncq), for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with:
    - Hemophilia A (congenital factor VIII deficiency) without factor VIII inhibitors, or
    - Hemophilia B (congenital factor IX deficiency) without factor IX inhibitors.
- Hemophilia A and hemophilia B are genetic bleeding disorders caused by a dysfunction or deficiency of coagulation factor VIII (FVIII) or IX (FIX), respectively. These bleeding episodes are typically managed by either on-demand, episodic treatment or prophylaxis using products containing FVIII or FIX, or a product that mimics a factor.
- Hympavzi is a first-in-class tissue factor pathway inhibitor (TFPI) antagonist. By reducing TFPI, Hympavzi increases the amount of thrombin, an enzyme that is critical in blood clotting.
    - Hympavzi is the first non-factor and once-weekly treatment for hemophilia B.
- The efficacy of Hympavzi was established in the BASIS study, an open-label, two-phase study in 116 adult and pediatric patients (aged 12 years and older and ≥ 35 kg) with severe hemophilia A without FVIII inhibitors or severe hemophilia B without FIX inhibitors. Following screening, patients entered a 6-month observation phase and were enrolled in two cohorts based on the factor replacement treatment they were receiving prior to study entry: on-demand or routine prophylaxis. Patients who completed the observation phase were to receive 12 months of Hympavzi. The efficacy of Hympavzi for each cohort was based upon the annualized bleeding rate (ABR) of treated bleeds during treatment with Hympavzi compared to ABR during the observational phase.
    - In the cohort of patients receiving on-demand factor-based therapy, the ABR was 38.00 during the observational 6-month period vs. 3.18 with Hympavzi prophylaxis treatment during the 12-month active treatment period (ratio 0.084, 95% CI: 0.059, 0.119; $p < 0.0001$). Hympavzi prophylaxis demonstrated superiority over on-demand factor-based therapy in incidences of treated bleeds.
    - In the cohort of patients receiving routine factor-based prophylaxis, the ABR was 7.85 during the observational 6-month period vs. 5.08 with Hympavzi prophylaxis treatment during the 12-month active treatment period (difference -2.77, 95% CI: -5.37, -0.16). Hympavzi prophylaxis demonstrated non-inferiority to routine prophylactic factor-based therapy as measured by ABR of treated bleeds.
- Warnings and precautions for Hympavzi include thromboembolic events; hypersensitivity; and embryofetal toxicity.
- The most common adverse reactions (≥ 3%) with Hympavzi use were injection site reaction, headache, and pruritus.
- The recommended loading dose of Hympavzi is 300 mg (two 150 mg subcutaneous injections). If more than one injection is required to deliver a complete dose, each injection should be administered at a different injection site.
- One week after the loading dose, maintenance dosing should be initiated at 150 mg every week by subcutaneous injection on the same day each week, at any time of day.

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  - A dose adjustment should be considered to 300 mg subcutaneous injection weekly in patients weighing greater than or equal to 50 kg when control of bleeding events is judged to be inadequate by the healthcare provider. Safety and efficacy of Hympavzi at doses above 300 mg weekly have not been established.

- Hympavzi is intended for use under the guidance of a healthcare provider. After proper training in subcutaneous injection technique, a patient may self-inject or the patient's caregiver may administer Hympavzi, if a healthcare provider determines that it is appropriate.

- Pfizer's launch plans for Hympavzi are pending. Hympavzi will be available as a 150 mg/mL single-dose prefilled syringe and pen.

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