Winrevair™ (sotatercept) – New orphan drug approval

- On March 26, 2024, Merck announced the FDA approval of Winrevair (sotatercept-csrk), for the treatment of adults with pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to increase exercise capacity, improve WHO functional class, and reduce the risk of clinical worsening events.

- PAH is a rare, progressive and life-threatening blood vessel disorder characterized by the constriction of small pulmonary arteries and elevated blood pressure in the pulmonary circulation. The disease progresses rapidly for many patients. PAH results in significant strain on the heart, leading to limited physical activity, heart failure and reduced life expectancy.

    — Approximately 40,000 people in the U.S. live with PAH. The five-year mortality rate for patients with PAH is approximately 43%.

- Winrevair is a first-in-class activin signaling inhibitor. Winrevair works by improving the balance between the pro- and anti-proliferative signaling to modulate the vascular cell proliferation underlying PAH.

- The efficacy of Winrevair was established in a double-blind, placebo-controlled study in 323 adult patients with PAH (WHO Group 1 Functional Class II or III). Patients were randomized to receive either Winrevair or placebo. Both groups received Winrevair or placebo in combination with background standard of care therapies. The primary endpoint was the change from baseline at week 24 in 6-Minute Walk Distance (6 MWD). The 6 MWD is a cardiopulmonary functional testing modality to assess the degree of functional impairment. A key secondary endpoint was risk of death from any cause and PAH clinical worsening events.

    — In the Winrevair group, the placebo-adjusted median increase in 6 MWD was 41 meters (95% CI: 28, 54; $p < 0.001$).
    — Patients treated with Winrevair had an 84% reduction in the risk of death from any cause or PAH clinical worsening events vs. placebo (hazard ratio 0.16, 95% CI: 0.08, 0.35; $p < 0.001$).

- Warnings and precautions include erythrocytosis, severe thrombocytopenia, serious bleeding, embryo-fetal toxicity, and impaired fertility.

- The most common adverse reactions (≥ 10%) with Winrevair use were headache, epistaxis, rash, telangiectasia, diarrhea, dizziness, and erythema.

- The recommended starting dose of Winrevair is 0.3 mg/kg by subcutaneous (SC) injection. The recommended target dose is 0.7 mg/kg every 3 weeks by SC injection.

    — Patients and caregivers may administer Winrevair when considered appropriate and when they receive training and follow-up from the healthcare provider on how to reconstitute, prepare, measure, and inject Winrevair.
    — Hemoglobin (Hgb) and platelet count should be obtained prior to the first dose of Winrevair. Treatment should not be initiated if platelet count is < 50,000/mm^3. Hgb and platelet count should be monitored before each dose or longer if values are unstable. Thereafter, Hgb and platelet count should be monitored periodically to determine if dose adjustments are required.

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- Merck plans to launch Winrevair by the end of April. Winrevair will be available in single-dose vials (45 mg or 60 mg).