Xolremdi™ (mavorixafor) – New orphan drug approval

- On April 29, 2024, the FDA announced the approval of X4 Pharmaceuticals' Xolremdi (mavorixafor), in patients 12 years of age and older with WHIM syndrome (warts, hypogammaglobulinemia, infections and myelokathexis) to increase the number of circulating mature neutrophils and lymphocytes.

- WHIM syndrome is a rare genetic disease that causes the body's immune system to not function properly. WHIM syndrome reduces the number of mature neutrophils and lymphocytes circulating within the body. While symptoms vary, patients with WHIM syndrome can have recurrent infections, including pneumonia, sinusitis, and skin infections and are at risk for life-threatening bacterial and viral infections.

    — It is estimated to occur in about 1 in 5 million live births. Approximately 60 cases have been reported in the medical literature.

- Xolremdi is a selective CXCR4 receptor antagonist. CXCR4 receptor stimulation by its ligand, CXCL12, has been shown to play a key role in the movement of white blood cells to and from the bone marrow compartment. Treatment with Xolremdi results in increased mobilization of neutrophils and lymphocytes from the bone marrow into peripheral circulation.

- The efficacy of Xolremdi was established in a randomized, double-blind, placebo-controlled study in 31 patients with WHIM syndrome. Patients were randomized to Xolremdi or placebo. Efficacy was based on improvement in absolute neutrophil counts (ANC), improvement in absolute lymphocyte counts (ALC), and a reduction in infections. ANC below 500 cells/μL and ALC below 1000 cells/μL are associated with an increased risk of infections.

    — The average length of time over 24 hours that ANC and ALC were above these levels was significantly longer with Xolremdi compared to the placebo group (15.0 hours compared to 2.8 hours for ANCs; 15.8 hours compared to 4.6 hours for absolute ALCs).
    — Xolremdi decreased the infection score by 40% over the 52-week treatment period compared to placebo.
    — Xolremdi did not improve warts.

- Xolremdi is contraindicated with drugs that are highly dependent on CYP2D6 for clearance.

- Warnings and precautions for Xolremdi include embryo-fetal toxicity and QTc interval prolongation.

- The most common adverse reactions (≥ 10% and at a frequency higher than placebo) with Xolremdi use were thrombocytopenia, pityriasis, rash, rhinitis, epistaxis, vomiting, and dizziness.

- The recommended dose of Xolremdi is:

    — Weight more than 50 kg: 400 mg orally once daily on an empty stomach after an overnight fast, and at least 30 minutes before food.
    — Weight less than or equal to 50 kg: 300 mg orally once daily on an empty stomach after an overnight fast, and at least 30 minutes before food.

- The wholesale acquisition cost (WAC) for Xolremdi is $496,400 annually for patients greater than 50 kilograms and $372,300 annually for patients less than or equal to 50 kilograms.

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- X4 Pharmaceuticals' launch plans for Xolremdi are pending. Xolremdi will be available as a 100 mg capsule.