Ultomiris® (ravulizumab-cwvz) – New formulation approval

- On July 22, 2022, the FDA approved a subcutaneous (SC) formulation of Alexion Pharmaceuticals' Ultomiris (ravulizumab-cwvz), for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA).

- Ultomiris was previously approved as an intravenous (IV) injection. In addition to the indications approved for the SC formulation, IV Ultomiris is also approved for:

    - Treatment of pediatric patients one month of age and older with PNH or aHUS to inhibit complement-mediated TMA
    - Treatment of adult patients with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor (AChR) antibody-positive.

- The efficacy of SC Ultomiris was established in a randomized, open-label study in 129 adult patients with PNH who were clinically stable after having been treated with Soliris® (eculizumab) for at least 3 months prior to study entry. The main outcome measure was the non-inferiority of C_{trough} of Ultomiris when administered SC vs. Ultomiris administered IV.

    - Treatment with SC Ultomiris achieved pharmacokinetic non-inferiority with a margin 0.80, compared with IV administered Ultomiris treatment for the serum ravulizumab-cwvz C_{trough} at day 71, with a geometric least squares mean ratio of 1.257 (90% CI: 1.160, 1.361). Serum free C5 concentrations were maintained below the target threshold (< 0.5 mcg/mL) in all patients throughout the one year of SC treatment.
    - No noticeable difference between the routes of administration was observed in change in lactate dehydrogenase, breakthrough hemolysis, transfusion avoidance, and hemoglobin stabilization, at day 71.

- Ultomiris carries a boxed warning for serious meningococcal infections.

    - Ultomiris is available only through a restricted program called the Ultomiris REMS.

- The recommended SC Ultomiris maintenance dose is 490 mg once weekly in adult patients greater than or equal to 40 kg body weight with PNH or aHUS. The 490 mg dose of Ultomiris is delivered using 2 on-body delivery systems. Each on-body delivery system consists of 1 on-body injector and 1 prefilled cartridge containing 245 mg of ravulizumab.

    - Refer to the Ultomiris drug label for treatment initiation instructions in patients who are complement inhibitor treatment-naïve or switching treatment from IV administration of Ultomiris or Soliris.
    - Ultomiris on-body delivery system is intended for administration by patients/caregivers. Patients/caregivers may administer after training from a healthcare provider.

- Refer to the Ultomiris drug label for dosing and administration information for IV Ultomiris.

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- Alexion's launch plans for Ultomiris SC are pending. Ultomiris SC will be available as a 245 mg/3.5 mL (70 mg/mL) solution in a single-dose prefilled cartridge for use only with supplied single-use on-body injector.