Onureg® (azacitidine oral tablets) – New orphan drug approval

- On September 1, 2020, Bristol-Myers Squibb announced the FDA approval of Onureg (azacitidine oral tablets), for the continued treatment of adult patients with acute myeloid leukemia (AML) who achieved first complete remission (CR) or CR with incomplete blood count recovery (CRi) following intensive induction chemotherapy and who are not able to complete intensive curative therapy.

- AML is characterized by rapid growth of abnormal cells in the bone marrow that interferes with normal blood cell production and function. Impaired red blood cells, white blood cells, and platelets can lead to signs of anemia, infection, and bleeding.

    - In 2017, an estimated 64,500 individuals were living with AML in the U.S.

- Onureg is a nucleoside metabolic inhibitor. The main mechanism of action is thought to be hypomethylation of DNA, as well as direct cytotoxicity to abnormal hematopoietic cells in the bone marrow.

    - Onureg is the first oral azacitidine product and FDA-approved therapy for continued AML therapy for patients in remission.
    - Azacitidine is also available generically as an injection (administered as an intravenous [IV] infusion or subcutaneous [SC] injection) for the treatment of myelodysplastic syndromes.

- The efficacy of Onureg was established in QUAZAR, a randomized, double-blind, placebo-controlled study in 472 patients with AML who were within 4 months of achieving first CR or CRi recovery with intensive chemotherapy. Patients were randomized to receive Onureg or placebo on days 1 through 14 of each 28-day cycle. The primary endpoint of the study was overall survival (OS).

    - The median OS for Onureg was 24.7 months (95% CI: 18.7, 30.5) vs. 14.8 months (95% CI, 11.7, 17.6) for placebo (Hazard Ratio 0.69; 95% CI: 0.55, 0.86; p = 0.0009).

- Warnings and precautions for Onureg include potential confusion with IV or SC formulations of azacitidine, myelosuppression, increased early mortality in patients with myelodysplastic syndromes, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 10%) with Onureg use were nausea, vomiting, diarrhea, fatigue/asthenia, constipation, pneumonia, abdominal pain, arthralgia, decreased appetite, febrile neutropenia, dizziness, and pain in extremity.

    - New or worsening Grade 3 or 4 neutropenia and thrombocytopenia occurred in 49% and 22% of patients who received Onureg, respectively. Complete blood counts should be monitored and Onureg doses modified per the recommendations in the Onureg prescribing information.

- The recommended dose of Onureg is 300 mg orally once daily with or without food on days 1 through 14 of each 28-day cycle, continuing until disease progression or unacceptable toxicity.

    - Due to the high risk of nausea and vomiting, an antiemetic is recommended before each dose for at least the first 2 cycles.
    - Onureg should not be split, crushed, or chewed.
    - Onureg should not be substituted for IV or SC azacitidine. The indications and dosing regimen for Onureg differ from that of IV or SC azacitidine.

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- Bristol Myers Squibb's launch plans for Onureg are pending. Onureg will be available as 200 mg and 300 mg tablets.