Inrebic® (fedratinib) – New orphan drug approval

- On August 16, 2019, the FDA announced the approval of Celgene's Inrebic (fedratinib), for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

- MF is a chronic disorder where scar tissue forms in the bone marrow and the production of the blood cells moves from the bone marrow to the spleen and liver, causing organ enlargement. It can cause extreme fatigue, shortness of breath, pain below the ribs, fever, night sweats, itching and bone pain.

    - When MF occurs on its own, it is called primary myelofibrosis.
    - Secondary MF occurs when there is excessive red blood cell production (polycythemia vera) or excessive platelet production (essential thrombocythemia) that evolves into MF.
    - In the U.S., between 16,000 and 18,500 are living with MF and 1.5 of every 100,000 people will be diagnosed with MF each year.

- Inrebic is an oral kinase inhibitor with activity against wild type and mutationally activated Janus associated kinase 2 (JAK2) and FMS-like tyrosine kinase 3. Abnormal activation of JAK2 is associated with myeloproliferative neoplasms, including MF and polycythemia vera.

- The efficacy of Inrebic was demonstrated in the JAKARTA study in 289 patients with intermediate-2 or high-risk MF, post-polycythemia vera MF or post-essential thrombocythemia MF with splenomegaly. Patients received Inrebic or placebo for at least six cycles. The efficacy of Inrebic was established based upon the proportion of patients achieving greater than or equal to a 35% reduction from baseline in spleen volume at the end of cycle 6 as measured by MRI or CT with a follow-up scan 4 weeks later.

    - A total of 37% of patients treated with Inrebic achieved a 35% reduction in spleen volume vs. 1% of placebo treated patients ($p < 0.0001$).

- Inrebic carries a boxed warning for encephalopathy including Wernicke's.

- Additional warnings and precautions of Inrebic include anemia and thrombocytopenia; gastrointestinal toxicity; hepatic toxicity; and amylase and lipase elevation.

- The most common adverse reactions (≥ 20%) with Inrebic use were diarrhea, nausea, anemia, and vomiting.

- The recommended dose of Inrebic is 400 mg orally once daily for patients with a baseline platelet count of greater than or equal to 50 x 10^9/L.

- Celgene's launch plans for Inrebic are pending. Inrebic will be available as 100 mg capsules.