Optum Rx®

Vonjo™ (pacritinib) – New orphan drug approval

- On February 28, 2022, CTI BioPharma announced the FDA approval of Vonjo (pacritinib), for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 × 10^9/L.
    - This indication is approved under accelerated approval based on spleen volume reduction. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Myelofibrosis is bone marrow cancer that results in formation of fibrous scar tissue and can lead to thrombocytopenia and anemia, weakness, fatigue and an enlarged spleen and liver.
    - In the U.S., there are approximately 21,000 patients with myelofibrosis, 7,000 of which have severe thrombocytopenia (defined as blood platelet counts below 50 × 10^9/L).
    - Severe thrombocytopenia is associated with poor survival and high symptom burden.
- Vonjo is a kinase inhibitor with activity against wild type Janus Associated Kinase 2 (JAK2), mutant $JAK2^{V617F}$ form and FMS-like tyrosine kinase 3 (FLT3), which contribute to signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. Myelofibrosis is often associated with dysregulated JAK2 signaling.
- The efficacy of Vonjo was established in PERSIST-2, a randomized study in 311 patients with intermediate or high-risk primary or secondary myelofibrosis with splenomegaly and a platelet count ≤ 100 × 10^9/L. Patients were randomized to receive Vonjo 400 mg once daily, Vonjo 200 mg twice daily, or best available therapy (BAT). The Vonjo dose of 400 mg once daily was not established as safe and is not an approved dosage regimen. The efficacy population was patients who had a platelet count < 50 x 10^9/L. The primary endpoint was the proportion of patients achieving ≥ 35% spleen volume reduction from baseline to week 24.
    - In patients with platelet counts < 50 x 10^9/L (n = 63), 29% of patients treated with Vonjo met the primary endpoint vs. 3% of patients treated with BAT (difference 25.9; 95% CI: 4.3, 44.5).
- As part of the accelerated approval, CTI BioPharma is required to describe a clinical benefit in a confirmatory trial. To fulfil this post-approval requirement, CTI BioPharma plans to complete the PACIFICA trial, with expected results in mid-2025.
- Vonjo is contraindicated in patients concomitantly using strong CYP3A4 inhibitors or inducers as these medications can significantly alter exposure to Vonjo, which may increase the risk of adverse reactions or impair efficacy.
- Warnings and precautions for Vonjo include hemorrhage; diarrhea; thrombocytopenia; prolonged QT interval; major adverse cardiac events; thrombosis; secondary malignancies; risk of infection; and interactions with CYP3A4 inhibitors or inducers.
- The most common adverse reactions (≥ 20%) with Vonjo use were diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema.

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- The recommended dosage of Vonjo is 200 mg orally twice daily. Patients who are on treatment with other kinase inhibitors before the initiation of Vonjo must taper or discontinue according to the prescribing information for that drug.

- CTI BioPharma launch plans for Vonjo are pending. Vonjo will be available as a 100 mg capsule