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FDA Approves First Drug for Myelofibrosis With Thrombocytopenia

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The US Food and Drug Administration (FDA) has granted accelerated approval for a new drug for the treatment of myelofibrosis, the first specifically for patients with low platelet counts.

Pacritinib (Vonjo, CTI BioPharma) is indicated for use in 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.

Pacritinib is a novel oral kinase inhibitor with specificity for activity against Janus associated kinase 2 (JAK2) and IRAK1, without inhibiting JAK1. The recommended dosage is 200 mg orally twice daily.

In the United States, there are approximately 21,000 patients with myelofibrosis, notes the manufacturer. About one third develop severe thrombocytopenia.

"Myelofibrosis with severe thrombocytopenia, defined as blood platelet counts below 50×10^9/L, has been shown to result in poor survival outcomes coupled with debilitating symptoms. Limited treatment options have rendered this disease as an area of urgent unmet medical need," commented John Mascarenhas, MD, associate professor, medicine, hematology, and medical oncology, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York City.

"I am pleased to see that a new, efficacious, and safe treatment option is now available for these patients," he said in a company press release.

Mascarenhas was the lead investigator of the phase 3 PERSIST-2 trial that was the basis for the approval. Results from the trial were published in 2018 in *JAMA Oncology* and reported in detail at the time by *Medscape Medical News*.

Authors of an accompanying editorial noted the trial was truncated after the FDA imposed a clinical hold on pacritinib in February 2016 after reports from an earlier trial, PERSIST-1, of patient deaths related to cardiac failure and arrest as well as intracranial hemorrhage. The clinical hold was lifted in January 2017 after the manufacturer provided the FDA with more mature data.

Despite the truncation, the PERSIST-2 trial provided sufficient data to obtain accelerated approval for the drug. The study compared pacritinib with best available therapy (BAT).

In the cohort of patients treated with pacritinib 200 mg twice daily, 29% of patients had a reduction in spleen volume of at least 35% compared with 3% of patients receiving BAT, which included ruxolitinib.

The company is now expected to demonstrate clinical benefit in a confirmatory trial and has the PACIFICA trial underway. Results are expected in mid-2025.

The most common adverse reactions (reported by ≥20% of patients) were diarrhea, thrombocytopenia, nausea, anemia, and peripheral edema. The most frequent serious adverse reactions (≥3%) were anemia, thrombocytopenia, pneumonia, cardiac failure, disease progression, pyrexia, and squamous cell carcinoma of the skin.