Indian Health Service
National Pharmacy and Therapeutics Committee

Pharmacovigilance Drug Safety Communication

Tofacitinib (Xeljanz®) may increase risk of serious heart-related problems and cancer

The FDA has issued a Drug Safety Communication (DSC) to alert clinicians about risks of heart-related problems and cancer with the use of tofacitinib. Tofacitinib belongs to a class of medications called Janus Kinase (JAK) Inhibitors. It is approved by the FDA for the treatment of rheumatoid and psoriatic arthritis in patients who do not respond well to methotrexate and for ulcerative colitis.

When first approved, the FDA required a safety trial of tofacitinib in patients with rheumatoid arthritis, age 50 and older, and with at least one cardiovascular risk factor. Interim analysis of this study showed an increased risk of blood clots and death among those receiving tofacitinib 10mg twice daily compared to treatment with either tofacitinib 5mg twice daily or a TNF blocker.

The tofacitinib boxed warning was modified to reflect these findings:

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY AND THROMBOSIS
- Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred.
- If a serious infection develops, interrupt XELJANZ/XELJANZ XR/XELJANZ Oral Solution until the infection is controlled.
- Prior to starting XELJANZ/XELJANZ XR/XELJANZ Oral Solution, perform a test for latent tuberculosis; if it is positive, start treatment for tuberculosis prior to starting XELJANZ/XELJANZ XR/XELJANZ Oral Solution.
- Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative.
- Thrombosis, including pulmonary embolism, deep venous thrombosis and arterial thrombosis have occurred in patients treated with XELJANZ and other Janus kinase inhibitors. Rheumatoid arthritis patients with at least one cardiovascular (CV) risk factor had a higher rate of all-cause mortality and thrombosis with XELJANZ 10 mg twice daily vs. 5 mg twice daily or TNF blockers.
- Lymphoma and other malignancies have been observed in patients treated with XELJANZ, including an increased rate of Epstein Barr Virus-associated post-transplant lymphoproliferative disorder.

Although the final results of this study are not yet available, preliminary results show an increased risk of heart-related problems and cancer with both the 5 and 10mg twice daily doses of tofacitinib. FDA is awaiting additional results from the trial and will communicate their final recommendations once the review is completed.

Current recommendations for Patients: Do not stop taking tofacitinib without first consulting with a health care professional, as doing so may worsen your condition. Talk to your health care professionals if you have any questions or concerns.

Current recommendations for health care professionals: Consider the benefits and risks of tofacitinib when deciding whether to prescribe or continue patients on the medicine. Continue to follow the recommendations in the tofacitinib prescribing information.

The complete Drug Safety Communication can be viewed on the FDA website.

To help the FDA track safety issues with tofacitinib, please report adverse events involving this or other medicines to the MedWatch program as recommended in the Indian Health Manual. Instructions for reporting can be found online at the NPTC Pharmacovigilance website.

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