U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz, Xeljanz XR) in rheumatoid arthritis patients; FDA to investigate

Safety Announcement

[2-25-2019] The U.S. Food and Drug Administration (FDA) is alerting the public that a safety clinical trial found an increased risk of blood clots in the lungs and death when a 10 mg twice daily dose of tofacitinib (Xeljanz, Xeljanz XR) was used in patients with rheumatoid arthritis (RA). FDA has not approved this 10 mg twice daily dose for RA; this dose is only approved in the dosing regimen for patients with ulcerative colitis.

In this ongoing safety trial required by FDA when it approved tofacitinib for RA, the drug manufacturer, Pfizer, is transitioning patients who were on the high 10 mg twice daily dose to the lower, currently approved dose of 5 mg twice daily. This trial will continue and is expected to be completed by the end of 2019. We are working with the manufacturer to evaluate other currently available safety information for tofacitinib and will update the public with any new information based on our ongoing review.

Health care professionals should follow the recommendations in the tofacitinib prescribing information for the specific condition they are treating. Monitor patients for the signs and symptoms of pulmonary embolism, and advise them to seek medical attention immediately if they experience them.

Patients should not stop or change your dose of tofacitinib without first talking to your health care professional, as doing so may worsen your condition. Patients taking tofacitinib should seek medical attention immediately if you experience symptoms of a blood clot in your lungs or other unusual symptoms such as:

- Sudden shortness of breath or difficulty breathing
- Chest pain or pain in your back
- Coughing up blood
- Excessive sweating
- Clammy or bluish colored skin

Tofacitinib works by decreasing the activity of the immune system. It was first approved in 2012 to treat adult patients with RA who did not respond well to the medicine methotrexate. In RA, the body attacks its own joints, causing pain, swelling, and loss of function. In 2017, we approved the medicine to treat patients with a second condition, psoriatic arthritis, who did not respond well to methotrexate or other similar medicines

called nonbiologic disease-modifying antirheumatic drugs (DMARDs). Psoriatic arthritis is a condition that also causes joint pain and swelling. In 2018, we approved tofacitinib to treat a condition called ulcerative colitis, which is a chronic, inflammatory bowel disease affecting the colon.

When FDA first approved tofacitinib, we required a clinical trial among patients with RA to evaluate the risk of heart-related events, cancer, and opportunistic infections with the medicine at two doses (10 mg twice daily and 5 mg twice daily) in combination with methotrexate in comparison to another drug called a tumor necrosis factor (TNF) inhibitor. RA patients in the trial were required to be at least 50 years old and have at least one cardiovascular risk factor. During the most recent analysis of the trial, an external data safety monitoring committee found an increased occurrence of blood clots in the lungs and death in patients treated with tofacitinib 10 mg twice daily compared to patients treated with tofacitinib 5 mg twice daily or a TNF inhibitor.

To help FDA track safety issues with medicines, we urge health care professionals and patients to report side effects involving tofacitinib or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

Related Information

The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective

Think It Through: Managing the Benefits and Risks of Medicines