Direct Healthcare Professional Communication

16May2023

Important Safety Information for Janus Kinase (JAK) Inhibitors - Xeljanz® (Tofacitinib)

Dear Healthcare Professional

In agreement with the Saudi Food and Drug Authority (SFDA), Pfizer would like to inform you of the following:

Summary:

- An increased incidence of malignancy, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE) and mortality has been observed in patients with rheumatoid arthritis (RA) with certain risk factors using JAKi treatment compared to TNFα inhibitors.
- These risks are considered class effects and relevant across all approved indications of JAKi in inflammatory and dermatologic diseases.
- These JAKi should only be used if no suitable treatment alternatives are available in patients:
    - *With a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors (such as current or past long-time smokers).*
    - *With malignancy risk factors (e.g. current malignancy or history of malignancy).*
    - *Who are 65 years of age and older*
- JAKi should be used with caution in patients with VTE risk factors other than those listed above.
- Dosing recommendations are revised for some patient groups with risk factors.
- Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.
- Patients should also be regularly re-evaluated to assess for changes in their venous thromboembolism (VTE) risk.
- Prescribers should discuss with patients the risks associated with the use of JAKi.

Background on the safety concern:

- Xeljanz® (Tofacitinib) approved therapeutic indications are Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Ulcerative Colitis, and Juvenile Idiopathic Arthritis (JIA)

- Based on the results from a post-marketing safety study of tofacitinib (ORAL Surveillance Study A3921133), the Saudi FDA has required a label update for all JAK inhibitors used in chronic inflammatory disorders. These updates include information about the risks of major adverse cardiovascular events (MACE), thrombosis, malignancy, all-cause mortality and use in the elderly.

- The ORAL Surveillance Study was a large, randomised trial designed to assess the safety profile of tofacitinib at two doses (5 mg twice daily and 10 mg twice daily) versus a tumour necrosis factor (TNF) inhibitor in patients with rheumatoid arthritis. Participants were 50 years of age and older with at least one additional cardiovascular risk factor.

- The study found higher incidence rates of MACE, thromboembolic events, malignancies (particularly lung cancer, lymphoma and non-melanoma skin cancer (NMSC)), serious infections and all-cause mortality in patients treated with tofacitinib compared to those treated with TNF inhibitors.

- The incidence rates of MACE and malignancies were higher with combined tofacitinib doses (5mg and 10mg) than with a TNF inhibitor (Hazard ratio 1.33 [95% CI 0.91 – 1.94] and 1.48 [95% CI 1.04 –2.09], respectively. MACE and malignancies were more common in patients 65 years and older and in patients who were current or past smokers. The increase in malignancies was mainly driven by higher rates of lung cancer and lymphoma. Adjudicated venous thromboembolism (VTE), serious infection and death from any cause were more frequent with the combined tofacitinib doses than with a TNF inhibitor.

Call for Reporting

Reporting of suspected adverse events is important for the monitoring of the safety of all medicines.

Suspected adverse reactions should be reported to:

- The National Pharmacovigilance Centre (NPC) at Saudi Food and Drug Authority (SFDA)

SFDA Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa/

- Pharmacovigilance Department in the company

E-mail: SAU.AEReporting@pfizer.com

Company Contacts

For more information, please contact Pfizer Medical Information:
MedInfoMEandAfrica@pfizer.com

Please note, you may receive a letter referring to this important information from multiple sponsors.

This letter is approved by the Executive Directorate of Pharmacovigilance at SFDA

Sincerely,
Arsalan, Mohammad Saeed
Senior Medical Manager,
Pfizer – Saudi Arabia