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Direct Healthcare-Professional Communication (DHPC)

Communication of new safety information: XELJANZ (tofacitinib): increased risk of venous thromboembolism and increased risk of serious and fatal infections

Dear Healthcare Provider,

Pfizer, in agreement with the Saudi Food and Drug Authority, would like to inform you of the following:

Summary:

- A dose-dependent increased risk of serious venous thromboembolism (VTE), including cases of pulmonary embolism (PE), some of which were fatal, and deep vein thrombosis (DVT) is observed in patients taking tofacitinib.
- Tofacitinib should be used with caution in patients with known risk factors for VTE, regardless of indication and dosage.
- Use of tofacitinib 10 mg twice daily for maintenance treatment in patients with ulcerative colitis (UC) should be limited to patients with loss of response and used for the shortest duration, with careful consideration of the benefits and risks for the individual patient.
- For treatment of rheumatoid arthritis and psoriatic arthritis, the recommended dose of 5 mg tablet twice daily or 11 mg prolonged-release tablet administered once daily, should not be exceeded.
- Inform patients of the signs and symptoms of VTE before they start tofacitinib therapy and advise them to seek prompt medical help if they develop these symptoms during treatment.

Background on the safety concern

Long-term safety study A3921133 in patients with rheumatoid arthritis:

This is an **ongoing** open-label clinical trial (N=4,362) to evaluate the cardiovascular safety of tofacitinib 5 mg twice daily and tofacitinib 10 mg twice daily, compared with a TNF inhibitor therapy in patients with rheumatoid arthritis who are 50 years of age or older and with at least one cardiovascular risk factor. After the interim results, study treatment with tofacitinib 10 mg twice daily was stopped and patients were switched to 5 mg twice daily because of a signal of VTE and all-cause mortality.

Venous thromboembolism (PE and DVT):
In the interim analysis, an increased and dose-dependent incidence of VTE was observed in patients treated with tofacitinib as compared to TNF inhibitors. The incidence rates (95%CI) for PE for tofacitinib 10 mg twice daily, 5 mg twice daily, and TNF inhibitors were 0.54 (0.32 – 0.87), 0.27 (0.12 – 0.52), and 0.09 (0.02 – 0.26) patients with events per 100 patient-years, respectively. The incidence rates (95%CI) for DVT for tofacitinib 10 mg twice daily, 5 mg twice daily, and TNF inhibitors were 0.38 (0.20 – 0.67), 0.30 (0.14 – 0.55), and 0.18 (0.07 – 0.39) patients with events per 100 patient-years, respectively. The HR for DVT with tofacitinib 10mg twice daily was 2.13 (0.80-5.69) and for 5 mg twice daily the HR was 1.66 (0.60-4.57), compared with TNF-inhibitors.

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Patient with ulcerative colitis (UC) and VTE:
In the UC ongoing extension trial, cases of PE and DVT have been observed in patients using tofacitinib 10 mg twice daily and with underlying VTE risk factor(s).

Serious infections:
For non-fatal serious infections, the incidence rates per 100 patients-years were 3.51 (2.93 - 4.16), 3.35 (2.78 - 4.01), and 2.79 (2.28 - 3.39), for tofacitinib 10 mg twice daily and 5 mg twice daily, and TNF inhibitors, respectively. In this study, which enrolled patients > 50 years and with CV risk factors, the risk of serious infections and fatal infections was further increased in elderly patients above 65 years of age, as compared to younger patients.

Mortality
In the interim analysis of study A3921133, increased mortality within 28 days of last treatment was observed in patients treated with tofacitinib compared to TNF-inhibitors. The incidence rates (95%CI) were 0.89 (0.59 – 1.29) for tofacitinib 10 mg twice daily, 0.57 (0.34 – 0.89) for tofacitinib 5 mg twice daily, and 0.27 (0.12 – 0.51) for TNF-inhibitors. Mortality was mainly due to cardiovascular events, infections and malignancies.

Patient safety is of the utmost importance to Pfizer and the company continually monitors the safety of its medicines. As such, we continue to work with regulatory agencies around the world on this safety signal. We wanted you to be aware of the emerging data especially the 10 mg twice daily dose arm of this ongoing RA study, so that you can consider this when counseling your patients on the use of Xeljanz.

For more information, please see the Xeljanz local full prescribing information enclosed or contact Pfizer Medical Information via:
MedInfoMEandAfrica@pfizer.com
https://pmiform.com/HCP/MID-EAST

Call for reporting:
As a reminder, there is a need to report any suspected adverse reactions to the

National Pharmacovigilance and Drug Safety Center (NPC):
E-mail: npc.drug@sfda.gov.sa
fax: +966 11 2057662
Website: https://ade.sfda.gov.sa/

Pharmacovigilance department in the company:
Email: SAU.AEReporting@Pfizer.com

Sincerely Yours,

Ahmed Hashiesh Medical Manager – Pfizer Saudi Arabia