Higher doses of Xeljanz for rheumatoid arthritis lead to increased risk of blood clots in lungs and death

08.04.2019 | P04/2019

Information on Xeljanz

- Xeljanz (tofacitinib) is authorised to treat adults with moderate to severe rheumatoid arthritis (a disease that causes inflammation of the joints) and psoriatic arthritis (red, scaly patches on the skin with inflammation of the joints). In these indications, Xeljanz is used together with methotrexate, after treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs) has not been satisfactory or has caused side effects
- In patients with rheumatoid arthritis, Xeljanz can also be used alone in patients who cannot take or are intolerant to methotrexate
- Xeljanz is also authorised to treat adults with moderate to severe ulcerative colitis (a disease-causing inflammation and ulcers in the lining of the gut), after treatment with other medicines has not been satisfactory, has stopped working or has caused side effects.

Information from the EMA about the safety concern

This review of Xeljanz is being carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) in the context of a safety signal. Following the initial results of the study A3921133 on Xeljanz, EMA is recommending to not exceed the recommended dose of 5 mg twice daily when treating rheumatoid arthritis. From the initial results it was shown an increased risk of blood clots in the lungs and death when the recommended dose of Xeljanz was doubled. While awaiting full results, EMA's recommendations are:

- Healthcare professionals should monitor patients for signs and symptoms of blood clots in the lungs
- Patients should not stop or change their dose of Xeljanz without talking to their doctor
- Patients should seek medical attention immediately if they experience symptoms such as difficulty breathing, pain in the chest or upper back and coughing up blood.

The PRAC's recommendation will be forwarded to the CHMP for endorsement.

In Malta

For Healthcare Professionals

- An increased risk of pulmonary embolism and overall mortality has been seen in a study with tofacitinib 10 mg twice daily in rheumatoid arthritis
- These results come from study A3921133, an ongoing open-label clinical trial evaluating the safety of tofacitinib 5 mg twice daily and tofacitinib 10 mg twice daily compared with a tumour necrosis factor (TNF) inhibitor in patients with rheumatoid arthritis. Patients in the study were 50 years of age or older with at least one additional cardiovascular risk factor
- The preliminary results of the study showed an overall incidence of pulmonary embolism to be 5-fold higher in the tofacitinib 10 mg twice daily arm of the study compared with the TNF inhibitor arm, and approximately 3-fold higher than tofacitinib in other studies across the tofacitinib program. Additionally, all-cause mortality in the 10 mg twice daily arm was higher compared with the tofacitinib 5 mg twice daily and the TNF inhibitor groups
- Patients receiving tofacitinib 10 mg twice daily in study A3921133 will have their dose reduced to 5 mg twice daily for the remaining duration of the study
- While further assessment of the study results continues, prescribers should continue to adhere to the authorised dose of 5 mg twice daily for the treatment of rheumatoid arthritis
- Patients receiving tofacitinib, irrespective of indication, should be monitored for the signs and symptoms of pulmonary embolism, and be advised to seek medical attention immediately if they experience them

A DHPC letter about the safety concern has been disseminated to HCPs in Malta. Archived DHPC letters are available online at http://www.medicinesauthority.gov.mt/dhpc

Advice for Patients

- A new ongoing study in patients with rheumatoid arthritis showed that when Xeljanz was given at a high dose of 10 mg twice daily there was an increased risk of blood clots in the lungs and death
- This dose is higher than the approved dose of 5 mg twice daily for rheumatoid arthritis
- If you are being treated with Xeljanz, you should not change the dose or stop taking the medicine without discussing with your doctor
- You should seek medical attention immediately if you experience the following symptoms which may be signs of a blood clot in your lungs: difficulty breathing, chest pain or pain in your upper back, coughing up blood, excessive sweating and bluish skin
- If you have any concern about your medicine, you should discuss it with a healthcare professional

For more information please see the European Medicines Agency's press release on Xeljanz.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Xeljanz (tofacinib). Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.>

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

Feedback:

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Pharmacovigilance Section

Post-Licensing Directorate

Medicines Authority

Sir Temi Żammit Buildings

Malta Life Sciences Park

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