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Xeljanz to be used with caution for all patients at high risk of blood clots

A review by EMA's safety committee (PRAC) has concluded that Xeljanz (tofacitinib) could increase the risk of blood clots in the lungs and in deep veins in patients who are already at high risk.

As a result, the PRAC is recommending that Xeljanz should be used with caution in patients at high risk of blood clots. In addition, the maintenance doses of 10 mg twice daily should not be used in patients with ulcerative colitis who are at high risk unless there is no suitable alternative treatment. Further, the PRAC is recommending that patients older than 65 years of age should be treated with Xeljanz only when there is no alternative treatment.

Patients at high risk of blood clots include those who have had a heart attack or have heart failure, cancer, inherited blood clotting disorders or a history of blood clots, as well as patients who take combined hormonal contraceptives, are receiving hormone replacement therapy, are undergoing major surgery or are immobile. Doctors should also consider other factors that may increase the risk of blood clots including age, obesity, diabetes, hypertension or smoking.

These recommendations follow the PRAC's review of an ongoing study (study A3921133) in patients with rheumatoid arthritis and an increased risk of cardiovascular disease. This study showed an increased risk of blood clots in deep veins and in the lungs with both the 5 mg and 10 mg twice daily doses of Xeljanz as compared with patients taking TNF-inhibitors. The PRAC also re-assessed additional data from earlier studies. All data combined showed that the risk of blood clots was higher in patients taking Xeljanz, especially with the 10 mg twice daily dose and in those being treated for an extended period. Results also showed a further increased risk of serious and fatal infections in patients older than 65 years of age.

The product information for Xeljanz will now be updated with new warnings and recommendations based on data from the study and will list blood clots as an uncommon side effect occurring in between 1 in 1,000 and 1 in 100 patients.

The PRAC has also recommended updating the physician's guide and the patient alert card with advice to minimise the risk of blood clots. Patients who have questions about their treatment or their risk of blood clots should contact their doctor.

The new recommendations replace the measures put in place at the start of the review in May 2019 when the PRAC recommended that doctors stop prescribing the 10 mg twice daily dose of Xeljanz for patients at high risk of blood clots in the lungs while it reviewed data from study A3921133.The PRAC's

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recommendations will now be sent to the EMA's human medicines committee (CHMP), which will adopt the Agency's final opinion.

More about the medicine

Xeljanz (tofacitinib) was first authorised in the EU on 22 March 2017 to treat adults with moderate to severe rheumatoid arthritis (a disease that causes inflammation of the joints). In 2018, its use was extended to treat adults with psoriatic arthritis (red, scaly patches on the skin with inflammation of the joints) and severe ulcerative colitis (a disease causing inflammation and ulcers in the lining of the gut). The active substance in Xeljanz, tofacitinib, works by blocking the action of enzymes known as Janus kinases. These enzymes play an important role in the process of inflammation that occurs in rheumatoid, psoriatic arthritis and ulcerative colitis. By blocking the enzymes' action, tofacitinib helps reduce the inflammation and other symptoms of these diseases.

Further information about the medicine can be found on the EMA website: ema.europa.eu/medicines/human/EPAR/xeljanz.

More about the procedure

The review of Xeljanz was initiated on 15 May 2019 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.