



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update as of 10 June 2022:

The European Commission has extended the scope of the review of JAK inhibitors to cover the use of Rinvoq for treating ulcerative colitis and the use of Olumiant for treating alopecia areata, which EMA's human medicines committee (CHMP) recently recommended for approval.

The scope is also extended to include the use of Rinvoq for treating non-radiographic axial spondyloarthritis, which the CHMP is currently evaluating.

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EMA starts safety review of Janus kinase inhibitors for inflammatory disorders

EMA's safety committee, PRAC, has started a review of the safety of Janus kinase (JAK) inhibitors used to treat several chronic inflammatory disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, ulcerative colitis and atopic dermatitis).

The review was prompted by the final results from a clinical trial ([study A3921133](#)) of the JAK inhibitor Xeljanz (tofacitinib). The results showed that patients taking Xeljanz for rheumatoid arthritis and who were at risk of heart disease were more likely to experience a major cardiovascular problem (such as heart attack, stroke or death due to cardiovascular disease) and had a higher risk of developing cancer than those treated with medicines belonging to the class of TNF-alpha inhibitors. The study also showed that compared with TNF-alpha inhibitors, Xeljanz was associated with a higher risk of death due to any cause, serious infections, and blood clots in the lungs and in deep veins (venous thromboembolism, VTE).

In addition, preliminary findings from an observational study involving another JAK inhibitor, Olumiant (baricitinib), also suggest an increased risk of major cardiovascular problems and VTE in patients with rheumatoid arthritis treated with Olumiant compared with those treated with TNF-alpha inhibitors.

In the treatment of inflammatory disorders, Olumiant and other JAK inhibitors work in a similar way to Xeljanz. PRAC will therefore carry out a review to determine whether these risks are associated with all

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JAK inhibitors authorised in the EU for the treatment of inflammatory disorders¹ and whether the marketing authorisations for these medicines should be amended.

Some measures to minimise these risks are already in place for Xeljanz as result of a [review](#) finalised in 2020, which analysed the interim results of study A3921133. In addition, the product information for Xeljanz was further updated in 2021 to reflect the increased risk of major cardiovascular problems and cancer observed after the release of additional data from this study.

More about the medicines

The Janus kinase inhibitors subject to this review¹ are used to treat several chronic inflammatory disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, ulcerative colitis and atopic dermatitis). The active substances in these medicines work by blocking the action of enzymes known as Janus kinases. These enzymes play an important role in the process of inflammation that occurs in these disorders. By blocking the enzymes' action, the medicines help reduce the inflammation and other symptoms of these disorders.

Some JAK inhibitors (Jakavi and Inrebic) are used to treat myeloproliferative disorders; at this stage the review will not include these medicines.

More about the procedure

The review of JAK inhibitors in the treatment of inflammatory disorders has been initiated at the request of the European Commission (EC) under [Article 20 of Regulation \(EC\) No 726/2004](#).

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. The PRAC recommendations will then be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt an opinion. The final stage of the review procedure is the adoption by the EC of a legally binding decision applicable in all EU Member States.

¹ Cibinqo (abrocitinib), Jyseleca (filgotinib), Olumiant (baricitinib), Rinvoq (upadacitinib) and Xeljanz (tofacitinib).