BlueCross BlueShield
Federal Employee Program

XELJANZ (tofacitinib tablets; oral solution)
XELJANZ XR (tofacitinib extended-release tablets)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Xeljanz/Xeljanz XR (tofacitinib) is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Janus kinase inhibitors inhibit one or more Janus family of enzymes (JAK1, JAK2, JAK3, TYK2), interfering with the JAK-STAT signaling pathway. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression (1).

Regulatory Status

FDA-approved indications: Xeljanz/Xeljanz XR is a Janus kinase (JAK) inhibitor indicated for the treatment of: (1)

1. Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers
2. Adult patients with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers
3. Adult patients with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers
4. Adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response or intolerance to one or more TNF blockers
5. Patients 2 years of age and older with active polyarticular course juvenile idiopathic arthritis (pcJIA) who have had an inadequate response to one or more TNF blockers

Limitations of Use:

Xeljanz/Xeljanz XR should not be used in combination with biological DMARDs or potent immunosuppressants such as azathioprine and cyclosporine (1).

Xeljanz/Xeljanz XR carries several boxed warnings: (1)

1. Serious infections
    a. There is an increased risk of serious infections including tuberculosis and bacterial, invasive fungi, viral and other opportunistic infections that may lead to hospitalization or

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death. If a serious infection develops, interrupt Xeljanz/Xeljanz XR until the infection is controlled. Prior to the initiation of Xeljanz/Xeljanz XR, a test for latent tuberculosis must be conducted. If the test is positive, start treatment for tuberculosis prior to starting Xeljanz/Xeljanz XR. Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative.

2. Mortality
    a. Rheumatoid arthritis patients with at least one cardiovascular (CV) risk factor had a higher rate of all-cause mortality and thrombosis with Xeljanz 10 mg twice daily vs. 5 mg twice daily or TNF blockers.
3. Malignancies
    a. Lymphoma and other malignancies have been observed in patients treated with Xeljanz/Xeljanz XR. Epstein Barr Virus- associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with Xeljanz/Xeljanz XR and concomitant immunosuppressive medications.
4. Major adverse cardiovascular events (MACE)
    a. RA patients 50 years of age and older with at least one CV risk factor, treated with Xeljanz, had a higher rate of MACE (defined as CV death, myocardial infarction, and stroke), compared to those treated with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue Xeljanz/Xeljanz XR use in patients that have experienced a myocardial infarction or stroke.
5. Thrombosis
    a. Thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis have occurred in patients treated with Xeljanz and other JAK inhibitors used to treat inflammatory conditions.

Pfizer shared results from a post-marketing required safety study of Xeljanz. These results showed a higher occurrence of malignancies and major adverse cardiovascular events (MACE) in those subjects with a higher prevalence of known risk factors (e.g., older age, smoking) (2).

The FDA has alerted the public that a safety clinical trial found an increased risk of blood clots in the lungs and death when a 10 mg twice daily dose of tofacitinib was used in patients with rheumatoid arthritis. FDA has not approved this 10 mg twice daily dose for RA; this dose is only approved in the

dosing regimen for patients with ulcerative colitis (3).

The safety and effectiveness of Xeljanz XR have not been established in pediatric patients. The safety and effectiveness of Xeljanz/Xeljanz oral solution in pediatric patients for indications other than pcJIA have not been established (1).

Summary

Xeljanz/Xeljanz XR (tofacitinib) is indicated for the treatment of adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), ulcerative colitis (UC), and patients 2 years of age and older with polyarticular course juvenile idiopathic arthritis (pcJIA). Xeljanz/Xeljanz XR has several boxed warnings including increased risk of serious infections, mortality, malignancies, MACE, and thrombosis. The safety and effectiveness of Xeljanz XR have not been established in pediatric patients. The safety and effectiveness of Xeljanz/Xeljanz oral solution in pediatric patients for indications other than pcJIA have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Xeljanz/Xeljanz XR while maintaining optimal therapeutic outcomes.

References

1. Xeljanz/Xeljanz XR [package insert]. New York, NY: Pfizer Labs; September 2024.
2. Pfizer shares co-primary endpoint results from post-marketing required safety study of Xeljanz (tofacitinib) in subjects with rheumatoid arthritis. January 27, 2021. Accessed at https://www.pfizer.com/news/press-release/press-release-detail/pfizer-shares-co-primary-endpoint-results-post-marketing
3. FDA Safety Announcement. Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz, Xeljanz XR) in rheumatoid arthritis patients. February 25, 2019. Accessed at https://www.fda.gov/Drugs/DrugSafety/ucm631871.htm