Xeljanz (tofacitinib)

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Policy
BCBSKC will provide coverage for Xeljanz® (tofacitinib) when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Xeljanz® (tofacitinib) requires prior authorization through the pharmacy services area.

Xeljanz® (tofacitinib) is considered medically necessary for rheumatoid arthritis in an adult after at least a 12-week treatment course with Humira® (adalimumab) and Enbrel (Etanercept) has not been effective.

When Policy Topic is not covered
Xeljanz® (tofacitinib) is considered not medically necessary in the following circumstances (this is not an exhaustive list of exclusions):

1. Concurrent Biologic Therapy. Xeljanz should not be administered in combination with a biologic for an inflammatory condition (e.g., Actemra [IV or SC], Kineret, Orecia [IV or SC], Rituxan, or a TNF inhibitor [such as Cimzia, Enbrel, Humira, Remicade, Simponi {SC}, or Simponi Aria]).¹ Co-administration with other potent immunosuppressive drugs has the risk of added immunosuppression and has not been evaluated in RA.

2. Concurrent use with Other Potent Immunosuppressants (e.g., azathioprine, tacrolimus, cyclosporine, mycophenolate mofetil).¹ Coadministration with other potent immunosuppressive drugs has the risk of added immunosuppression and has not been evaluated in RA. Note: This does NOT exclude use of Xeljanz with MTX; Xeljanz has been evaluated with background MTX, leflunomide, or combinations of DMARDs containing MTX and/or leflunomide.¹⁵

3. Plaque Psoriasis. More data are needed. A 12-week Phase IIb dose-ranging study demonstrated efficacy of Xeljanz over placebo in patients with moderate-to-severe plaque psoriasis (n = 197), as assessed by the proportion of patients achieving a ≥ 75% decrease in the Psoriasis Area and Severity Index (PASI 75) score at Week 12.¹⁶ Long-term studies are required to demonstrate on-going efficacy.

4. Renal Transplantation. More data are needed. A Phase IIb study in kidney transplant patients (n = 331) found Xeljanz was equivalent to cyclosporine in preventing acute rejection.¹⁷ however, based on Phase IIb studies, there are concerns of Epstein Barr Virus-
associated post-transplant lymphoproliferative disorder (PTLD) in certain transplant patients receiving Xeljanz.\textsuperscript{1,17}

5. **Ulcerative Colitis.** More data are needed. A Phase II study in adults with ulcerative colitis ($n = 194$) found significantly more patients achieved a clinical response (defined by requirements for decrease in Mayo score) at Week 8 when treated with Xeljanz 15 mg twice daily (BID) compared with placebo (61\% vs. 42\%, respectively; $P < 0.001$).\textsuperscript{18} Clinical remission (defined as a Mayo score \leq 2 with no subscore \geq 1) at Week 8 occurred in significantly more patients treated with Xeljanz 3 mg, 10 mg, and 15 mg BID compared with placebo (33\%, 48\%, 41\%, and 10\%, respectively; $P = 0.01$ for the 3 mg dose compared to placebo, $P < 0.001$ for other doses compared to placebo).

**Description of Procedure or Service**
Xeljanz is an inhibitor of the Janus kinases (JAK) pathways approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate (MTX).\textsuperscript{1} It is a targeted synthetic disease-modifying antirheumatic drugs (DMARD) that may be used either as monotherapy or in combination with MTX or other conventional synthetic DMARDs for RA. Xeljanz should not be used in combination with other potent immunosuppressants (e.g., azathioprine and cyclosporine) or biologic DMARDs (e.g., Actemra\textsuperscript{®} [tocilizumab intravenous [IV] infusion, tocilizumab for subcutaneous {SC} injection], Kineret\textsuperscript{®} [anakinra for SC injection], Orencia\textsuperscript{®} [abatacept for SC injection, abatacept for IV infusion], Rituxan\textsuperscript{®} [rituximab for IV infusion], or a tumor necrosis factor [TNF] inhibitor [such as Cimzia\textsuperscript{®} {certolizumab pegol for SC injection}, Enbrel\textsuperscript{®} {etanercept for SC injection}, Humira\textsuperscript{®} {adalimumab for SC injection}, Remicade\textsuperscript{®} {infliximab for IV infusion}, Simponi\textsuperscript{™} {golimumab for SC injection}, Simponi\textsuperscript{®} Aria\textsuperscript{™} {golimumab for IV infusion}]). Xeljanz inhibits JAK, an intracellular enzyme that transmits signals on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STAT) which then modulate intracellular activity such as gene expression. The efficacy of Xeljanz over placebo was established in seven pivotal studies that included a variety of clinical scenarios, including Xeljanz as monotherapy or in combination with MTX or other DMARDs and in patients who had failed a TNF inhibitor.\textsuperscript{2-10}

**Considerations**
This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Hayes Medical Technology Directory, Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

**Rationale**
Xeljanz has Boxed Warnings regarding serious infections leading to hospitalization or death, tuberculosis, and risks of malignancy/lymphoproliferative disorders.\textsuperscript{1} In general, the rates of serious infection reported with Xeljanz are consistent with rates reported in the literature for RA patients treated with biologic and non-biologic DMARDs; however, the rates of herpes zoster infections in Xeljanz-treated patients were increased compared with placebo- and Humira-treated patients.\textsuperscript{11} During a 12-month safety analysis, exposure-adjusted incidence of malignancies was reported to be similar in patients treated with Xeljanz 5 mg and Humira.\textsuperscript{12} However, the rate of malignancies increased numerically in patients treated with Xeljanz in the
long-term extension studies. At this time, it is unknown if increasing exposure to Xeljanz increases the risk of malignancy.

Other Warnings/Precautions include viral reactivation, gastrointestinal perforation, laboratory parameters/monitoring (i.e., lymphocytes, neutrophils, hemoglobin, liver enzymes, and lipids), vaccinations, and hepatic impairment. Prior authorization is recommended for prescription benefit coverage of Xeljanz because of the specialized skills required for evaluation and diagnosis of patients treated with Xeljanz as well as the monitoring required for adverse events and long-term efficacy.

References

12. Division of Pulmonary, Allergy and Rheumatology Products, Center for Drug Evaluation & Research, FDA. FDA briefing information for the Arthritis Advisory Committee. NDA 203214: tofacitinib for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had inadequate response to one or more disease modifying anti-rheumatic drugs. Silver Springs, MD; May 9, 2012. Accessed November 6, 2012. Available at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Art hritisAdvisoryCommittee/UCM302958.pdf


Billing Coding/Physician Documentation Information
N/A Oral Xeljanz is a pharmacy benefit

Additional Policy Key Words
N/A

Related Topics
N/A

Policy Implementation/Update Information
03/2014 New policy

This Medical Policy is designed for informational purposes only and is not an authorization, an explanation of benefits, or a contract. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there is any exclusion or other benefit limitations applicable to this service or supply. Medical technology is constantly changing and Blue Cross and Blue Shield of Kansas City reserves the right to review and
revise medical policy. This information is proprietary and confidential and cannot be shared without the written permission of Blue Cross and Blue Shield of Kansas City.