Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

Xeljanz/Xeljanz XR (tofacitinib)

Policy Number: 5.01.560
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Last Review: 6/2023
Next Review: 6/2024

Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) 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/XR® (tofacitinib) requires prior authorization through the pharmacy services area.

Xeljanz®/Xeljanz XR (tofacitinib) is considered medically necessary for **rheumatoid arthritis in adults** after a trial of **one or more** TNF inhibitors (Cimzia, Humira, Simponi/ARIA).

Xeljanz®/Xeljanz XR (tofacitinib) is considered medically necessary for **psoriatic arthritis in adults** after at least a 12-week treatment course of **one** first line agents (Cimzia, Humira, Simponi/ARIA) has not been effective.

Xeljanz®/Xeljanz XR (tofacitinib) is considered medically necessary for moderate to severe **ulcerative colitis in adults** after at least a 12-week treatment course of **two** or more TNF inhibitors (e.g., Humira, Simponi/ARIA, Stelara) has not been effective.

Xeljanz® (tofacitinib) is considered medically necessary for the treatment of active **polyarticular course juvenile idiopathic arthritis** in patients ≥2 years of age at least a 12-week treatment course of Humira.

Xeljanz®/Xeljanz XR (tofacitinib) is considered medically necessary for the treatment of **ankylosing spondylitis in adults** after a trial of **one** or more TNF inhibitors (Cimzia, Humira, Simponi/ARIA).

Xeljanz® (tofacitinib) is considered medically necessary for **alopecia universalis (totalis) in adults.**

When Policy Topic is not covered

BlueKC may impose administrative limits on the quantity or frequency by which a drug may be dispensed. These limits will be based on recommendations of the drug manufacturer or by community physicians and pharmacists.

Xeljanz/Xeljanz XR has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent Use with a Biologic or with a Targeted Synthetic DMARD.** Xeljanz/XR should not be administered in combination with a biologic used for an inflammatory condition (see APPENDIX for examples).[1] Combination therapy is generally not recommended due to a potential for a higher rate of adverse effects with combinations and lack of evidence supporting additive efficacy. There are no data evaluating combination of Xeljanz/XR with a targeted synthetic DMARD (e.g., Otezla); therefore, safety and efficacy of this combination is unknown.

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/Xeljanz XR with MTX; Xeljanz/Xeljanz XR has been evaluated with background MTX, leflunomide, or combinations of DMARDs containing MTX and/or leflunomide.[1-7]

3. **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;[11] 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.[1,11]

Considerations

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

Description of Procedure or Service

Xeljanz/Xeljanz XR 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).[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. 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 TNFi.[1-6] Efficacy studies were not required for approval of Xeljanz XR because it was determined that Xeljanz XR (11 mg once daily) is pharmacokinetically equivalent to Xeljanz 5 mg administered twice daily.[1] Xeljanz/XR is also indicated in adults with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to MTX or other DMARDs. The recommended dose of Xeljanz is 5 mg BID; the dose of Xeljanz XR is 11 mg QD. In PsA, Xeljanz/XR should be given in combination with nonbiologic DMARDs.

Disease Overview

Inflammatory conditions are chronic, systemic, autoimmune, inflammatory disorders of unknown origin characterized by inflammation.[12] RA causes joint swelling, stiffness, and

tenderness which may lead to cartilage damage, bone erosions, and joint destruction, and is often associated with significant activity limitations and disability. Compared with patients who do not have RA, mortality is increased in patients with established RA with approximately 40% of deaths in the RA population attributed to cardiovascular causes such as ischemic heart disease or stroke.[13] RA is associated with a decreased quality of life and can contribute to reduced employment rates and increased costs of care.[12] In RA, Xeljanz/Xeljanz XR inhibits JAK, an intracellular enzyme that transmits signals on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function.[1] JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STAT) which then modulate intracellular activity such as gene expression. Inhibition of JAK1 and JAK3 block multiple cytokines resulting in modulation of the immune response involved in RA. Similar to RA, inhibition of JAKs with Xeljanz/XR modulates psoriatic inflammation in articular and extra-articular locations in patients with PsA.

Guidelines
Guidelines from the American College of Rheumatology (ACR) [2015] have TNFis (e.g., Cimzia® [certolizumab pegol SC injection], etanercept SC products [e.g., Enbrel®], adalimumab SC products [e.g., Humira®], infliximab IV products [e.g., Remicade®, Renflexis, Inflectra], Simponi® [golimumab SC injection], Simponi Aria® [golimumab IV infusion]) and non-TNF biologics (i.e., Actemra® [tocilizumab IV infusion, tocilizumab SC injection], Orencia® [abatacept IV infusion, abatacept SC injection], rituximab IV products [e.g., Rituxan®]), administered with or without MTX, equally positioned as a recommended therapy following a trial of a csDMARD (e.g., MTX, leflunomide, hydroxychloroquine, sulfasalazine).[9] The guidelines note that Xeljanz has potential longer-term safety concerns. Also, there is less clinical experience and concern of the actual benefit/risk profile with Xeljanz. Xeljanz is most commonly listed as a treatment option following at least two biologics; it is also among the treatment options for patients with established RA, following failure of DMARD monotherapy. Note that guidelines for PsA have not yet been updated to include Xeljanz/XR.

Rationale

Xeljanz/Xeljanz XR has Boxed Warnings regarding increased risk of developing serious infections which may lead to hospitalization or death.[1] Patients who develop a serious infection should interrupt treatment with Xeljanz/XR until infection is controlled. Patients should be tested for tuberculosis (TB) prior to starting therapy and monitored during treatment with Xeljanz/XR. Lymphoma and other malignancies have been observed in patients taking Xeljanz/XR. Epstein Barr virus-associated post-transplant lymphoproliferative disorder has been observed at a higher rate in patients with a renal transplant who were treated with Xeljanz and concomitant immunosuppressant medications.

The condition of alopecia universalis (totalis) is a rare condition for which Xeljanz has been shown to be safe and effective in small trials. As this is a rare condition, there will not be enough patients to perform random controlled trials.

Warnings and Precautions

• Hypersensitivity: Hypersensitivity reactions, including angioedema and urticaria, have occurred; discontinue therapy and evaluate cause for serious reactions.

• Interstitial lung disease: Interstitial lung disease (ILD) has been reported; patients developing ILD were receiving concomitant therapy associated with ILD (eg,

methotrexate). Use with caution in patients with risk/history of ILD (Xeljanz Canadian product monograph).

References

1. Xeljanz®/Xeljanz XR tablets/extended release tablets [prescribing information]. New York, NY: Pfizer Inc; December 2017.
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3. Kremer J, Li ZG, Hall S, et al. Tofacitinib in combination with nonbiologic disease-modifying antirheumatic drugs in patients with active rheumatoid arthritis: a randomized trial. *Ann Intern Med*. 2013;159(4):253-261.
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5. van der Heijde D, Tanaka Y, Fleischmann R, et al. Tofacitinib (CP-690,550) in patients with rheumatoid arthritis receiving methotrexate: twelve-month data from a twenty-four-month phase III randomized radiographic study. *Arthritis Rheum*. 2013;65(3):559-570.
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8. 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 October 18, 2016.
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Other References Utilized

- Sandborn WJ, Su C, Sands BE, et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2017;376(18):1723-1736.

- Panés J, Su C, Bushmakin AG, et al. Randomized trial of tofacitinib in active ulcerative colitis: analysis of efficacy based on patient-reported outcomes. *BMC Gastroenterol*. 2015;15:14.
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Billing Coding/Physician Documentation Information

Xeljanx/XR is a pharmacy benefit

Policy Implementation/Update Information

03/2014	New policy
03/2015	Reviewed – no changes made
03/2016	Changed titled to include XR; changed review date to 07/2016 due to upcoming formulary decisions
03/2017	Removed prerequisite requirement of Humira and Enbrel
07/2017	Reviewed – no changes made
08/2017	Added treatment is alopecia universalis as a medically necessary condition
06/2018	Reviewed – no changes made
07/2018	Added UC and PsA indications
06/2019	Reviewed – no changes made
09/2019	Added Humira to the preferred step for UC
01/2020	Reviewed to ensure consistency with Optum Step changes, no changes needed
06/2020	Annual review – no changes made
03/2021	Added indication for polyarticular course juvenile idiopathic arthritis
06/2021	Annual review – no changes made
12/2021	Added new indication for ankylosing spondylitis
05/2022	Updated step criteria for all indications
06/2022	For AS indication, changed from requiring 2 preferred agents to say one or more TNFi
06/2023	Added Warnings and Precautions

APPENDIX

Brand (generic name)	Mechanism of Action
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF
Enbrel® (etanercept for SC injection)	Inhibition of TNF
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF
Humira® (adalimumab for SC injection)	Inhibition of TNF
Amjevita® (adalimumab-atto for SC injection)	Inhibition of TNF
Cyltezo® (adalimumab-adbm for SC injection)	Inhibition of TNF
Simponi® (golimumab for SC injection)	Inhibition of TNF
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF
Remicade® (infliximab for IV infusion)	Inhibition of TNF
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator
Orencia® (abatacept for SC injection)	T-cell costimulation modulator
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23
Siliq™ (brodalumab SC injection)	Inhibition of IL-17
Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A
Tremfya™ (guselkumab for SC injection)	Inhibition of IL-23
Ilumya™ (tildrakizumab-asmn for SC injection)	Inhibition of IL-23
Otezla® (apremilast tablets)	Inhibition of PDE4
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways

SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin;PDE4 – Phosphodiesterase 4; JAK – Janus kinase.