



# Louisiana

## tofacitinib (Xeljanz<sup>®</sup>/Xeljanz<sup>®</sup> XR)

Policy # 00352

Original Effective Date: 05/22/2013

Current Effective Date: 01/01/2021

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

### When Services May Be Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

#### Rheumatoid Arthritis

Based on review of available data, the Company may consider the use of tofacitinib tablets (Xeljanz<sup>®</sup>/Xeljanz<sup>®</sup> XR)<sup>‡</sup> for the treatment of adult patients with moderately to severely active rheumatoid arthritis to be **eligible for coverage**.\*\*

#### Patient Selection Criteria

Coverage eligibility for tofacitinib tablets (Xeljanz/Xeljanz XR) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has a diagnosis of moderately to severely active rheumatoid arthritis; AND
- Patient had an inadequate response or intolerance to methotrexate; AND
- Requested drug is NOT being used in combination with biologic disease modifying anti-rheumatic drugs (DMARDs), such as adalimumab (Humira<sup>®</sup>)<sup>‡</sup> or etanercept (Enbrel<sup>®</sup>)<sup>‡</sup>, OR potent immunosuppressants such as azathioprine and cyclosporine, OR drugs such as apremilast (Otezla<sup>®</sup>)<sup>‡</sup>; AND
- Requested drug may be used alone or in combination with methotrexate or other NON-biologic DMARDs; AND
- Patient has a negative TB (tuberculosis) test (e.g., purified protein derivative [PPD], blood test) prior to treatment.

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## **Psoriatic Arthritis**

Based on review of available data, the Company may consider the use of tofacitinib tablets (Xeljanz/Xeljanz XR) for the treatment of adult patients with active psoriatic arthritis to be **eligible for coverage.\*\***

### **Patient Selection Criteria**

Coverage eligibility for tofacitinib tablets (Xeljanz/Xeljanz XR) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has a diagnosis of active psoriatic arthritis; AND
- Patient had an inadequate response or intolerance to methotrexate OR any other non-biologic DMARD; AND
- Requested drug is NOT being used in combination with biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR drugs such as apremilast (Otezla); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

## **Ulcerative Colitis**

Based on review of available data, the Company may consider the use of tofacitinib tablets (Xeljanz/Xeljanz XR) for the treatment of adult patients with moderately to severely active ulcerative colitis to be **eligible for coverage.\*\***

### **Patient Selection Criteria**

Coverage eligibility for tofacitinib tablets (Xeljanz/Xeljanz XR) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has a diagnosis of moderately to severely active ulcerative colitis; AND
- Patient has failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine (6-MP) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND  
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met).*

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- Patient has failed treatment with adalimumab (Humira) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of adalimumab (Humira) will be ineffective or cause an adverse reaction to the patient; AND  
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met.)*
- Requested drug is NOT being used in combination with biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR drugs such as apremilast (Otezla); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

### **Polyarticular Juvenile Idiopathic Arthritis**

Based on review of available data, the Company may consider the use of tofacitinib tablets or oral solution (Xeljanz) for the treatment of patients with active polyarticular juvenile idiopathic arthritis to be **eligible for coverage.\*\***

### **Patient Selection Criteria**

Coverage eligibility for tofacitinib tablets and oral solution (Xeljanz) will be considered when all of the following criteria are met:

- Patient has a diagnosis of active polyarticular juvenile idiopathic arthritis; AND
- Patient is 2 years of age or older; AND
- Patient has failed treatment with one or more DMARDs unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND  
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary\*\* if not met.)*
- Requested drug is NOT being used in combination with biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR drugs such as apremilast (Otezla); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

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## When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of tofacitinib tablets (Xeljanz/Xeljanz XR) for moderately to severely active ulcerative colitis when the member has NOT failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine OR when the member has not failed treatment with Humira after at least two months of therapy to be **not medically necessary.\*\***

Based on review of available data, the Company considers the use of tofacitinib tablets and oral solution (Xeljanz) for the treatment of polyarticular juvenile idiopathic arthritis when the member has NOT failed treatment with one or more DMARDs to be **not medically necessary.\*\***

## When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of tofacitinib tablets and oral solution (Xeljanz/Xeljanz XR) when patient selection criteria are not met (with the exception of the criterion considered to be **not medically necessary\*\***) to be **investigational.\***

Based on review of available data, the Company considers the use of tofacitinib oral solution (Xeljanz) for any indication other than polyarticular juvenile idiopathic arthritis to be **investigational.\***

Based on review of available data, the Company considers the use of tofacitinib (Xeljanz XR) for the treatment of polyarticular juvenile idiopathic arthritis to be **investigational.\***

## Background/Overview

The active ingredient in the Xeljanz line of products, tofacitinib, is an inhibitor of Janus kinases (JAKs) and is the first inhibitor of the JAKs pathway approved for adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate as well as for the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other disease modifying anti-rheumatic drugs. Xeljanz

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tablets and Xeljanz XR tablets are approved for the treatment of adults with moderately to severely active ulcerative colitis who have had an inadequate response or who are intolerant to TNF (tumor necrosis factor) inhibitors. Xeljanz tablets (NOT XR) and Xeljanz oral solution are approved for the treatment of active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older. Janus kinases 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. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Xeljanz/Xeljanz XR modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. Janus kinase enzymes transmit cytokine signaling through pairing of JAKs (e.g., JAK1/JAK3, JAK1/JAK2, JAK1/TyK2, JAK2/JAK2).

Xeljanz is provided as 5 mg and 10 mg tablets as well as a 1 mg/mL oral solution. Xeljanz XR is provided as 11 mg and 22 mg extended release tablets. The 22 mg XR tablets are only for the ulcerative colitis indication. Xeljanz/Xeljanz XR should not be used in combination with biologic DMARDs or immunosuppressants such as azathioprine and cyclosporine. In regard to rheumatoid arthritis and psoriatic arthritis, the dose of Xeljanz is 5 mg tablets by mouth twice daily with or without food and the dose of Xeljanz XR is 11 mg once daily. For ulcerative colitis induction dosing, Xeljanz is dosed as 10 mg tablets twice daily for at least 8 weeks and Xeljanz XR is dosed as 22 mg once daily for 8 weeks; then patients need to be evaluated and transitioned to maintenance therapy depending on therapeutic response. If needed, these doses can be continued for a maximum of 16 weeks. Discontinue after 16 weeks of Xeljanz 10 mg tablets twice daily or Xeljanz XR 22 mg once daily if adequate therapeutic benefit is not achieved. Maintenance dosing is Xeljanz 5 mg tablets twice daily or Xeljanz XR 11 mg once daily. For patients with loss of response during maintenance treatment, Xeljanz 10 mg tablets twice daily or Xeljanz XR 22 mg once daily may be considered and limited to the shortest duration. Use the lowest effective dose to maintain response. For polyarticular juvenile idiopathic arthritis, the dose of Xeljanz tablets and oral solution is 5 mg twice daily or weight based equivalent dosing given twice daily (as found in the package insert).

## **Rheumatoid Arthritis**

Rheumatoid Arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an

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autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as DMARDs are used to treat this condition.

### **Psoriatic Arthritis**

Psoriatic Arthritis is an arthritis that is often associated with psoriasis of the skin. Typically, first line treatments such as DMARDs are used to treat this condition.

### **Polyarticular Juvenile Idiopathic Arthritis**

Polyarticular juvenile idiopathic arthritis includes the inflammation of joints and presence of arthritis in children. Polyarticular juvenile idiopathic arthritis typically occurs in a symmetrical manner with knees, wrists, and ankles most frequently affected. However certain subgroups of children do have predominantly asymmetrical involvement. Typically, first line treatments such as DMARDs are used to treat this condition.

### **Disease-Modifying Anti-Rheumatic Drugs (DMARDs)**

Disease-modifying anti-rheumatic drugs are used for the treatment of rheumatoid arthritis as well as other inflammatory conditions. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine
- gold compounds

### **Ulcerative Colitis**

Ulcerative colitis is a chronic, episodic, inflammatory disease of the large intestine and rectum characterized by bloody diarrhea. This disease usually begins in the rectal area and may eventually extend through the entire large intestine. Repeated episodes of inflammation lead to thickening of the wall of the intestine and rectum with scar tissue. Death of colon tissue or sepsis may occur with severe disease. The goals of treatment are to control the acute attacks, prevent recurrent attacks and promote healing of the colon. Hospitalization is often required for severe attacks. Typically, first line treatments such as corticosteroids, 6-mercaptopurine and azathioprine are used to treat this condition.

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## **FDA or Other Governmental Regulatory Approval**

### **U.S. Food and Drug Administration (FDA)**

Xeljanz tablets were approved in November of 2012 and Xeljanz XR was approved in 2016 by the FDA for the treatment of moderately to severely active rheumatoid arthritis in adult patients who have had an inadequate response to or an intolerance to methotrexate. In 2018, both products gained an indication for the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to methotrexate or other disease modifying anti-rheumatic drugs. Xeljanz tablets (not the XR version) gained an indication for the treatment of adults with moderately to severely active ulcerative colitis. In mid 2019, the indication for ulcerative colitis was changed to add the requirement of an inadequate response or intolerance to TNF blockers. In late 2019, the XR version of Xeljanz was approved for the treatment of ulcerative colitis. In late 2020, Xeljanz tablets and the newly created Xeljanz oral solution were approved for the treatment of polyarticular juvenile idiopathic arthritis.

## **Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

### **Rheumatoid Arthritis**

Xeljanz in this section refers to the tablets. Xeljanz was studied in five pivotal trials. The trials varied in length from 6-24 months and the number of participants in the five trials varied from 399 subjects to nearly 800 subjects. All participants had moderate to severe rheumatoid arthritis. Varying by trial, participants had failed therapy with non-biologic or biologic DMARDs. In all trials, patients received either Xeljanz 5 mg by mouth twice daily or Xeljanz 10 mg by mouth twice daily. Xeljanz was studied as either monotherapy or in combination with non-biologic DMARDs such as methotrexate, depending on the trial. The comparator groups varied by trial but included placebo, placebo plus methotrexate, and adalimumab (Humira). In all trials, Xeljanz had a statistically

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significant greater number of subjects that achieved American College of Rheumatology (ACR20) response rates versus placebo. However, other outcome measures such as the Health Assessment Questionnaire Disability Index (HAQ-DI) and the Disease Activity Score (DAS28-4[ESR]) varied as to whether Xeljanz showed a statistically significant difference throughout the various trials.

### **Psoriatic Arthritis**

Xeljanz in this section refers to the tablets. Xeljanz was studied in two multicenter, randomized, double-blind, placebo-controlled trials (PsA-I and PsA-II) for psoriatic arthritis. The primary endpoints for both trials were the ACR20 response and the change from baseline to month 3 in HAQ-DI. At month 3, patients treated with either Xeljanz 5 mg or 10 mg twice daily had higher ( $p \leq 0.05$ ) response rates versus placebo for ACR20, ACR50, and ACR70 in Study PsA-I and for ACR20 and ACR50 in Study PsA-II; ACR70 response rates were also higher for both Xeljanz 5 mg or 10 mg twice daily versus placebo in Study PsA-II, although the differences versus placebo were not statistically significant ( $p > 0.05$ ).

### **Ulcerative Colitis**

Xeljanz in this section refers to the tablets. Xeljanz was studied in two identical induction trials (UC-I and UC-II) in 1139 patients. The dosage studied was 10 mg twice daily or placebo. The trial included subjects that had failed or were intolerant to at least one of the following treatments: oral or intravenous corticosteroids, azathioprine, 6 mercaptopurine, or tumor necrosis factor (TNF) blockers. The primary endpoint of Study UC-I and Study UC-II was the proportion of patients in remission at week 8. In UC-I, at week 8, 18% of the study population was in remission in the Xeljanz group vs. 8% in the placebo group. In UC-II, at week 8, 17% of the study population was in remission in the Xeljanz group vs. 4% in the placebo group.

A total of 593 patients who completed the induction trials (UC-I or UC-II) and achieved clinical response were re-randomized with 1:1:1 treatment allocation ratio to Xeljanz 5 mg twice daily, Xeljanz 10 mg twice daily, or placebo for 52 weeks in Study UC-III. The primary endpoint was the proportion of patients in remission at week 52. At week 52, 34% in the Xeljanz 5 mg twice daily group, 41% in the Xeljanz 10 mg twice daily group, and 11% in the placebo group reached the primary endpoint.

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## **Polyarticular Juvenile Idiopathic Arthritis**

The efficacy of Xeljanz/Xeljanz oral solution for polyarticular juvenile idiopathic arthritis was assessed in Study pcJIA-I, a 44-week, two-part study (consisting of an 18-week, open-label, run-in phase, followed by a 26-week double-blind, placebo-controlled, randomized withdrawal phase) in patients 2 years to 17 years of age. Patients received Xeljanz/Xeljanz oral solution (dosed at 5 mg twice daily or body weight-based equivalent twice daily) for 18 weeks (run-in phase) followed by randomization to either Xeljanz/Xeljanz oral solution (dosed at 5 mg twice daily or body weight-based equivalent twice daily) or placebo for 26 weeks (double-blind phase). Only patients who achieved at least a JIA (Juvenile Idiopathic Arthritis) ACR30 response at the end of the run-in phase were randomized (1:1) to the double-blind phase. Treatment with a stable dose of methotrexate was permitted but was not required during the study. Concurrent use of biologics or DMARDs other than methotrexate was not permitted in the study.

A total of 225 polyarticular juvenile idiopathic arthritis patients with active polyarthritis were enrolled in the run-in phase. Of the 225 patients, 173 (76.9%) patients achieved JIA ACR30 response at week 18 and were randomized into the double-blind phase to either active Xeljanz/Xeljanz oral solution (n=88) or placebo (n=85). At the conclusion of the 18-week, open-label, run-in phase, pediatric ACR 30/50/70 responses were 77%, 70%, and 49%, respectively.

The primary endpoint was the occurrence of disease flare at week 44 relative to the double-blind phase baseline at week 18. Disease flare was defined (according to Pediatric Rheumatology Collaborative Study Group (PRCSG)/Pediatric Rheumatology International Trials Organization (PRINTO) Disease Flare criteria) as worsening of  $\geq 30\%$  in 3 or more of the 6 JIA core response variables with no more than 1 of the remaining JIA core response variables improving by  $\geq 30\%$ .

Xeljanz/Xeljanz oral solution treated patients experienced significantly fewer disease flares at week 44 compared to placebo-treated patients (31% [27/88] vs. 55% [47/85]; difference in proportions - 25% [95% CI: -39%, -10%]; p=0.0007).

## **References**

1. Xeljanz [package insert]. Pfizer. New York, New York. Updated October 2020.
2. Pfizer, Inc. Advisory Committee meeting: tofacitinib for the treatment of rheumatoid arthritis; NDA 203214. Briefing document for the Arthritis Advisory Committee. May 9, 2012.

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Accessed November 6, 2012. Available at: <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM302960.pdf>

3. 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. Available at:
4. <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ArthritisAdvisoryCommittee/UCM302958.pdf>
5. Fleischmann R, Kremer J, Cush J, et al. Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. *N Engl J Med.* 2012;367(6):495-507.
6. Kremer J, Li ZG, Hall S, et al. Tofacitinib (CP-690, 550), an oral JAK inhibitor, in combination with traditional DMARDs: Phase 3 study in patients with active rheumatoid arthritis with inadequate response to DMARDs [abstract LB0005]. *Ann Rheum Dis.* 2011;70(Suppl3):170.
7. Strand V, Kremer JM, Li ZG, et al. Tofacitinib (CP-690,550) in combination with traditional disease-modifying anti-rheumatic drugs: Phase 3 study patient-reported outcomes in patients with active rheumatoid arthritis and an inadequate response to disease-modifying anti-rheumatic drugs [abstract 2627]. *Arthritis Rheum.* 2011;63(Suppl):1032.
8. van Vollenhoven RF, Fleischmann R, Cohen S, et al. Tofacitinib or adalimumab versus placebo in rheumatoid arthritis. *N Engl J Med.* 2012;367(6):508-519.
9. van der Heijde D, Tanaka Y, Fleischmann R, et al. Tofacitinib (CP-690,550) in patients with rheumatoid arthritis on methotrexate: 12-Month data from a 24-month Phase 3 randomized radiographic study. *Arthritis Rheum.* 2013 Jan 24. [Epub ahead of print]
10. van der Heijde D, Tanaka Y, Fleischmann R, et al. Tofacitinib (CP-690,550), an oral Janus kinase inhibitor, in combination with methotrexate reduced the progression of structural damage in patients with rheumatoid arthritis: a 24-month phase 3 study [abstract 2592]. *Ann Rheum Dis.* 2011;70 (Suppl):1017.
11. Burmester GR, van der Heijde D, Strand V, et al. Effects of tofacitinib on patient-reported outcomes in patients with active rheumatoid arthritis receiving stable-dose methotrexate: results of two Phase 3 studies [abstract 1283]. Presented at: the ACR/ARHP Annual Scientific Meeting Annual; Washington, DC; November 9-14, 2012.

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12. van der Heijde D, Tanaka Y, Fleischmann R, et al. Tofacitinib, an oral Janus kinase inhibitor, in combination with methotrexate reduced the progression of structural damage in patients with rheumatoid arthritis: Year 2 efficacy and safety results from a 24-month Phase 3 study [abstract 1277]. Presented at: the ACR/ARHP Annual Scientific Meeting Annual; Washington, DC; November 9-14, 2012.
13. Burmester G, Blanco R, Charles-Schoeman C, et al. Tofacitinib (CP-690,550), an oral Janus kinase inhibitor, in combination with methotrexate, in patients with active rheumatoid arthritis with an inadequate response to tumor necrosis factor inhibitors: a 6-month Phase 3 study [abstract 718]. *Arthritis Rheum.* 2011;63(Suppl):279.
14. Fleischmann R, Cutolo M, Genovese MC, et al. Phase IIb dose-ranging study of the oral JAK inhibitor tofacitinib (CP-690,550) or adalimumab monotherapy versus placebo in patients with active rheumatoid arthritis with an inadequate response to disease-modifying antirheumatic drugs. *Arthritis Rheum.* 2012;64(3):617-629.
15. Kremer JM, Cohen S, Wilkinson BE, et al. A phase IIb dose-ranging study of the oral JAK inhibitor tofacitinib (CP-690,550) versus placebo in combination with background methotrexate in patients with active rheumatoid arthritis and an inadequate response to methotrexate alone. *Arthritis Rheum.* 2012;64(4):970-981.
16. Wollenhaupt J, Silverfield JC, Lee EB, et al. Tofacitinib, an oral Janus kinase inhibitor, in the treatment of rheumatoid arthritis: open-label, long-term extension safety and efficacy up to 48 months [abstract 1282]. Presented at: the ACR/ARHP Annual Scientific Meeting Annual; Washington, DC; November 9-14, 2012.
17. Lee EB, Fleischmann R, Hall S, et al. Radiographic, clinical and functional comparison of tofacitinib monotherapy versus methotrexate in methotrexate-naïve patients with rheumatoid arthritis [abstract 2486]. Presented at: the ACR/ARHP Annual Scientific Meeting Annual; Washington, DC; November 9-14, 2012.
18. Sandborn WJ, Ghosh S, Panes J, et al. Tofacitinib, an oral Janus kinase inhibitor, in active ulcerative colitis. *N Engl J Med.* 2012;367(7):616-624.
19. Vincenti F, Tedesco Silva H, Busque S, et al. Randomized phase 2b trial of tofacitinib (CP-690,550) in de novo kidney transplant patients: efficacy, renal function and safety at 1 year. *Am J Transplant.* 2012;12(9):2446-2456.
20. Papp KA, Menter A, Strober B, et al. Efficacy and safety of tofacitinib, an oral Janus kinase inhibitor, in the treatment of psoriasis: a Phase 2b randomized placebo-controlled dose-ranging study. *Br J Dermatol.* 2012;167(3):668-677.

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21. Sandborn WJ, Ghosh S, Panes J, et al. Phase 2 randomized study of cp-690,550 an oral janus kinase inhibitor in active crohn's disease [abstract 745]. *Gastroenterology*. 2011;140(Suppl)S124.
22. Pfizer. Pharmacokinetics Of CP-690,550 In Pediatric Patients With Juvenile Idiopathic Arthritis (JIA). In: *ClinicalTrials.gov* [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2012 Nov 20]. Available from: <http://www.clinicaltrials.gov/ct2/show?term=tofacitinib&rank=14> NLM Identifier: NCT01513902.
23. Pfizer. Long-term safety study of CP-690,550 in patients with juvenile idiopathic arthritis. In: *ClinicalTrials.gov* [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2012 Nov 20]. Available from: <http://www.clinicaltrials.gov/ct2/show?term=tofacitinib&rank=16> NLM Identifier: NCT01500551.
24. Humira<sup>®</sup> solution for injection [package insert]. North Chicago, IL: Abbott Laboratories; September 2012.
25. Data on file. Xeljanz reports of malignancy. Pfizer.
26. Available at: <https://accountcenter.pfizer.com/Status.aspx?pageName=Confirm&status=1>
27. Singh JA, Cameron DR. Summary of AHRQ's comparative effectiveness review of drug therapy for rheumatoid arthritis (RA) in adults--an update. *J Manag Care Pharm*. 2012;18(4 Supp C):S1-18.
28. Smolen JS, Aletaha D, Bijlsma JW, et al; T2T Expert Committee. Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis*. 2010;69:631-637.
29. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken)*. 2012;64(5):625-639.
30. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. *Ann Rheum Dis*. 2010;69(6):964-975.
31. Bykerk V. Unmet needs in rheumatoid arthritis. *J Rheumatol Suppl*. 2009;82:42-46.
32. Furst DE, Keystone EC, Braun J, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2011. *Ann Rheum Dis*. 2012;71 Suppl 2:i2-45.
33. Cimzia<sup>®</sup> for injection [package insert]. Smyrna, GA: UCB, Inc.; August 2012.

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- 34. Enbrel<sup>®</sup> powder for injection [package insert]. Seattle, WA: Immunex Corporation; December 2011.
- 35. Remicade<sup>®</sup> for intravenous infusion [package insert]. Malvern, PA: Centocor, Inc; October 2011.
- 36. Simponi<sup>®</sup> injection [package insert]. Horsham, PA: Centocor Ortho Biotech Inc; December 2011.
- 37. Campbell J, Lowe D, Sleeman MA. Developing the next generation of monoclonal antibodies for the treatment of rheumatoid arthritis. *Br J Pharmacol.* 2011;162(7):1470-1484.
- 38. Actemra<sup>®</sup> injection for intravenous infusion [package insert]. South San Francisco, CA: Genentech; October 2012.
- 39. Kineret<sup>®</sup> injection [package insert]. Thousand Oaks, CA: Amgen Inc.; December 15, 2009.
- 40. Orencia<sup>®</sup> for injection [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2011.
- 41. Rituxan<sup>®</sup> injection [package insert]. South San Francisco, CA: Genentech, Inc; July 2012.
- 42. Cohen S, Radominsk SC, asavatanabodee P, et al. Tofacitinib (CP-690,550), an oral Janus kinase inhibitor: analysis of infections and all-cause mortality across Phase 3 and long-term extension studies in patients with rheumatoid arthritis [abstract 409]. Presented at: the ACR/ARHP Annual Scientific Meeting Annual; Chicago, IL; November 5-9, 2011.
- 43. FDA approves Xeljanz for rheumatoid arthritis [press release]. Silver Springs, MD: FDA; November 6, 2012. Updated November 13, 2012. Available at: <http://www.fda.gov/NewsEvents/Newsroom/Press Announcements /ucm327152.htm>

## Policy History

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- 05/02/2013 Medical Policy Committee review
- 05/22/2013 Medical Policy Implementation Committee approval. New policy.
- 10/10/2013 Medical Policy Committee review
- 10/16/2013 Medical Policy Implementation Committee approval. Added criteria that requires Humira AND Enbrel prior to use of Xeljanz for rheumatoid arthritis. Created a not medically necessary section to reflect changes.
- 10/02/2014 Medical Policy Committee review
- 10/15/2014 Medical Policy Implementation Committee approval. No change to coverage.

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10/08/2015	Medical Policy Committee review
10/21/2015	Medical Policy Implementation Committee approval. No change to coverage.
10/06/2016	Medical Policy Committee review
10/19/2016	Medical Policy Implementation Committee approval. Added info regarding the new dosage form, Xeljanz XR.
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Removed the requirement for use of Humira and Enbrel prior to Xeljanz/XR.
04/05/2018	Medical Policy Committee review
04/18/2018	Medical Policy Implementation Committee approval. Added indication for psoriatic arthritis.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. Added indication for Xeljanz for ulcerative colitis and updated the background info, rationale/source sections.
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. Removed required drugs prior to Xeljanz/XR for psoriatic arthritis and removed Humira prior to Xeljanz for ulcerative colitis.
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. Changed Xeljanz criteria for ulcerative colitis to include a trial and failure of Humira for two months to more closely reflect the change in the FDA indication.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. Added information regarding the 22 mg dosage of Xeljanz XR. Removed the investigational statement regarding use of Xeljanz XR in ulcerative colitis and updated the investigational statement to reflect that the use of the 22 mg dosage for any indication other than ulcerative colitis will be considered investigational. Updated relevant background information.
12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. Added a new indication, polyarticular juvenile idiopathic arthritis, to the policy and updated relevant background information.

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Next Scheduled Review Date: 12/2021

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  - 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
  - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  - 3. Reference to federal regulations.

\*\*Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

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For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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**NOTICE:** If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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