LOUISIANA BLUE

tofacitinib (Xeljanz®/Xeljanz® XR)

Policy # 00352
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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®/Xeljanz® XR)‡ for the treatment of 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 has failed treatment with one or more traditional disease modifying anti-rheumatic drugs (DMARDs), such as methotrexate, 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 selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has failed treatment with etanercept (Enbrel®)‡ OR adalimumab (Humira®, Simlandi®, adalimumab-adaz)‡ after at least TWO months of therapy 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. A failure of a different tumor necrosis factor (TNF) inhibitor would also count towards this criterion (e.g., adalimumab [other than those listed above], [certolizumab pegol [Cimzia®]‡, golimumab [Simponi® or Simponi Aria®]‡, infliximab [Remicade®, Renflexis®, etc.]‡); AND
  *(Note: This specific patient selection 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, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR drugs such as apremilast (Otezla®)‡; AND
- Patient has a negative TB (tuberculosis) test (e.g., purified protein derivative [PPD], blood test) prior to treatment.

Psoriatic Arthritis

Based on review of available data, the Company may consider the use of tofacitinib tablets (Xeljanz/Xeljanz XR) for the treatment of 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 has failed treatment with one or more traditional DMARDs, such as methotrexate, 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 selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Humira, Simlandi®, adalimumab-adaz) after at least TWO months of therapy 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. A failure of a different TNF inhibitor would also count towards this criterion (e.g., adalimumab [other than those listed above], certolizumab pegol [Cimzia], golimumab [Simponi or Simponi Aria], infliximab [Remicade, Renflexis, etc.]); AND
  *(Note: This specific patient selection 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, biosimilars) 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 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 selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has failed treatment with adalimumab (Humira, Simlandi®, adalimumab-adaz) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of adalimumab (Humira, Simlandi®, adalimumab-adaz) will be ineffective or cause an adverse reaction to the patient. A failure of a different TNF inhibitor would also count towards this criterion (e.g., adalimumab [other than those listed above], golimumab [Simponi] or infliximab [Remicade, Renflexis, etc.]); AND
  *(Note: This specific patient selection 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, biosimilars) 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 traditional DMARDs, such as methotrexate, 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 selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Humira, Simlandi®, adalimumab-adaz) after at least TWO months of therapy 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. A failure of a different TNF inhibitor would also count towards this criterion (e.g., adalimumab [other than those listed above], golimumab [Simponi Aria] or infliximab [Remicade, Renflexis, etc.]); AND
  *(Note: This specific patient selection 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, biosimilars) 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.

Ankylosing Spondylitis

Based on review of available data, the Company may consider the use of tofacitinib tablets (Xeljanz/Xeljanz XR) for the treatment of patients with active ankylosing spondylitis 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 active ankylosing spondylitis; AND
- Patient has failed treatment with non-steroidal anti-inflammatory drugs (NSAIDs) unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has failed treatment with etanercept (Enbrel) OR adalimumab (Humira, Simlandi®, adalimumab-adaz) after at least TWO months of therapy 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. A failure of a different TNF inhibitor would also count towards this criterion (e.g., adalimumab [other than those listed above], certolizumab pegol [Cimzia], golimumab [Simponi or Simponi Aria], infliximab [Remicade, Renflexis, etc.]); AND

*(Note: This specific patient selection 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, biosimilars) 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.

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 patient has NOT failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine OR when the patient has not failed treatment with adalimumab (Humira, Simlandi, adalimumab-adaz) 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 patient has NOT failed treatment with one or more traditional DMARDs to be **not medically necessary.****

Based on review of available data, the Company considers the use of tofacitinib tablets (Xeljanz/Xeljanz XR) for the treatment of rheumatoid arthritis or psoriatic arthritis when the patient has NOT failed treatment with one or more traditional DMARDs to be **not medically necessary.****

Based on review of available data, the Company considers the use of tofacitinib tablets (Xeljanz/Xeljanz XR) for the treatment of ankylosing spondylitis when the patient has NOT failed treatment with NSAIDs to be **not medically necessary.****

Based on review of available data, the Company considers the use of tofacitinib tablets (Xeljanz/Xeljanz XR) and tofacitinib oral solution (Xeljanz) for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, or polyarticular juvenile idiopathic arthritis when the patient has NOT failed treatment with etanercept (Enbrel) OR adalimumab (Humira, Simlandi®, adalimumab-adaz) after at least TWO months of therapy 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.***

tofacitinib (Xeljanz®/Xeljanz® XR)

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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 was the first inhibitor of the JAKs pathway approved for patients with inflammatory conditions. Xeljanz 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 one or more TNF (tumor necrosis factor) blockers, for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more TNF blockers, for the treatment of adult patients with psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers, and for the treatment of adult patients with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers. 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 who have had an inadequate response or intolerance to one or more TNF blockers. 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, psoriatic arthritis, and ankylosing spondylitis, 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 autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Psoriatic Arthritis
Psoriatic arthritis is an arthritis that is often associated with psoriasis of the skin. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

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 traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Traditional Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
Traditional 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.

Ankylosing Spondylitis
Ankylosing spondylitis is a chronic inflammatory disease that affects the joints between the vertebrae of the spine, and the joints between the spine and the pelvis. It eventually causes the affected vertebrae to fuse or grow together. Nonsteroidal anti-inflammatory drugs, such as ibuprofen or naproxen, are used to reduce inflammation and pain associated with the condition. Corticosteroid therapy or medications to suppress the immune system may be prescribed to control various symptoms.

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. In late 2021, Xeljanz and Xeljanz XR gained a new indication for the treatment of adults with ankylosing spondylitis. At the same time as the ankylosing spondylitis indication addition, language was added to all of the existing indications requiring an inadequate response or intolerance to a TNF blocker.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to 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 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.

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 ≥ 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 ≥ 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).

Ankylosing Spondylitis
Xeljanz in this section refers to the tablets. The efficacy and safety of Xeljanz was assessed in one placebo-controlled confirmatory trial (Study AS-I). Patients had active disease as defined by both Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and back pain score (BASDAI question 2) of greater or equal to 4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease modifying anti-rheumatic drug (DMARD) therapy. Study AS-I was a randomized, double-blind, placebo-controlled, 48-week clinical trial in 269 adult patients who had an inadequate response (inadequate clinical response or intolerance) to at least 2 NSAIDs. Patients were randomized and treated with Xeljanz 5 mg twice daily or placebo for 16 weeks of blinded treatment and then all received treatment of Xeljanz 5 mg twice daily for additional 32 weeks. The primary endpoint was to evaluate the proportion of patients who achieved an Assessment in Spondyloarthritis International Society 20 (ASAS20) response at week 16. Patients treated with Xeljanz 5 mg twice daily achieved greater improvements in ASAS20 and ASAS40 responses compared to placebo at week 16 (56% in the Xeljanz group vs. 29% in the placebo group).

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tofacitinib (Xeljanz®/Xeljanz® XR)

Policy # 00352
Original Effective Date: 05/22/2013
Current Effective Date: 04/01/2025

Policy History

Original Effective Date: 05/22/2013
Current Effective Date: 04/01/2025

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.
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

tofacitinib (Xeljanz®/Xeljanz® XR)

Policy # 00352
Original Effective Date: 05/22/2013
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12/09/2020	Medical Policy Implementation Committee approval. Added a new indication, polyarticular juvenile idiopathic arthritis, to the policy and updated relevant background information.
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. No change to coverage.
01/06/2022	Medical Policy Committee review
01/12/2022	Medical Policy Implementation Committee approval. Added a requirement for the trial and failure of Humira or Enbrel prior to the Xeljanz line of products in rheumatoid arthritis, psoriatic arthritis, and polyarticular juvenile idiopathic arthritis. Added a new FDA approved indication, ankylosing spondylitis, along with subsequent patient selection criteria. Updated background information to reflect the FDA label changes. Switched traditional DMARD usage to a not medically necessary denial due to label changes.
03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Clarified that other TNF failures can count in lieu of a trial and failure of Humira or Enbrel, where applicable.
03/02/2023	Medical Policy Committee review
03/08/2023	Medical Policy Implementation Committee approval. No change to coverage.
03/07/2024	Medical Policy Committee review
03/13/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/06/2025	Medical Policy Committee review
03/12/2025	Medical Policy Implementation Committee approval. Updated criteria to reflect availability of Humira biosimilars where applicable.

Next Scheduled Review Date: 03/2026

*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 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.

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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.