PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Xeljanz/Xeljanz XR Prior Authorization Policy
- Xeljanz®/Xeljanz XR (tofacitinib tablets, oral solution/extended-release tablets – Pfizer)

REVIEW DATE: 08/31/2022

OVERVIEW

Xeljanz/Xeljanz XR is an inhibitor of the Janus kinases pathways.[1] Xeljanz/Xeljanz XR tablets are approved for the following uses:

- **Ankylosing spondylitis**, in adults with active disease who have had an inadequate response or intolerance to one or more tumor necrosis factor inhibitors (TNFis).
- **Polyarticular juvenile idiopathic arthritis (JIA)**, in patients ≥ 2 years of age with active disease who have had an inadequate response or intolerance to one or more TNFis. Note: This indication is for Xeljanz only (not the XR formulation).
- **Psoriatic arthritis**, in adults with active disease who have had an inadequate response or intolerance to one or more TNFis. In psoriatic arthritis, Xeljanz/Xeljanz XR should be used in combination with a conventional synthetic disease-modifying antirheumatic drug (DMARD).
- **Rheumatoid arthritis**, in adults with moderately to severely active disease who have had an inadequate response or intolerance to one or more TNFis.
- **Ulcerative colitis**, in adults with moderately to severely active disease who have had an inadequate response or who are intolerant to one or more TNFis.

Xeljanz oral solution is only indicated for **polyarticular JIA**.

For all indications, Xeljanz/Xeljanz XR is not recommended for use in combination with biologics or potent immunosuppressants such as azathioprine or cyclosporine.

Guidelines

Guidelines for the treatment of inflammatory conditions recommend use of Xeljanz/Xeljanz XR.

- **Ankylosing Spondylitis:** Guidelines from the American College of Rheumatology (ACR)/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (2019) recommend TNFis as the initial biologic.[8] In those who are secondary non-responders to a TNFi, a second TNFi is recommended over switching out of the class. Both TNFis and interleukin-17 blockers are recommended over Xeljanz/Xeljanz XR.
- **JIA:** Xeljanz is not addressed in ACR/Arthritis Foundation guidelines for the treatment of JIA (2019) specific to juvenile non-systemic polyarthritis, sacroiliitis, and enthesitis.[2] TNFis are the biologics recommended for polyarthritis, sacroiliitis, and enthesitis. Actemra® (tocilizumab intravenous infusion, tocilizumab subcutaneous injection) and Orencia® (abatacept intravenous infusion, abatacept subcutaneous injection) are also among the biologics recommended for polyarthritis. Biologics are recommended following other therapies (e.g., following DMARDs for active polyarthritis or following a nonsteroidal anti-inflammatory drug for active JIA with sacroiliitis or enthesitis). However, there are situations where initial therapy with a biologic may be preferred over other conventional therapies (e.g., if there is involvement of high-risk joints such as the cervical spine, wrist, or hip; high disease activity; and/or those judged to be at high risk of disabling joint damage).

- **Psoriatic arthritis:** Guidelines from ACR (2018) recommend TNFis over other biologics and Xeljanz for use in treatment-naïve patients with psoriatic arthritis and in those who were previously treated with an oral therapy.[3]
- **Rheumatoid arthritis:** Guidelines from ACR (2021) recommend addition of a biologic or a targeted synthetic DMARD for a patient taking the maximum tolerated dose of methotrexate who is not at target.[4]
- **Ulcerative colitis:** Guidelines from the American College of Gastroenterology for ulcerative colitis (2019) note that the following agents can be used for induction of remission in moderately to severely active disease: budesonide extended-release tablets; oral or intravenous systemic corticosteroids, Entyvio® (vedolizumab intravenous infusion), Xeljanz, or TNFis.[5] Guidelines from the American Gastroenterological Association (2020) recommend Xeljanz only after failure of or intolerance to a TNFi.[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Xeljanz/Xeljanz XR. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of a patient treated with Xeljanz/Xeljanz XR as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Xeljanz/Xeljanz XR to be prescribed by or in consultation with a physician who specializes in the condition being treated.

All reviews for use of Xeljanz/Xeljanz XR for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Xeljanz/Xeljanz XR is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Ankylosing Spondylitis.** Approve Xeljanz/Xeljanz XR tablets (not oral solution) for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets ONE of the following (a or b):
       - **a)** Patient has had a 3-month trial of at least ONE tumor necrosis factor inhibitor; OR
       - **b)** Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND

         Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for rheumatoid arthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.
     - **iii.** The medication is prescribed by or in consultation with a rheumatologist.
   - **B)** Patient is Currently Receiving Xeljanz/Xeljanz XR. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has been established on therapy for at least 6 months; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Xeljanz/Xeljanz XR); OR
Note: Examples of objective measures include Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), Health Assessment Questionnaire for the Spondylarthropathies (HAQ-S), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

b) Compared with baseline (prior to initiating Xeljanz/Xeljanz XR), patient experienced an improvement in at least one symptom, such as decreased pain or stiffness, or improvement in function or activities of daily living.

2. Juvenile Idiopathic Arthritis (JIA). Approve Xeljanz tablets (not the Xeljanz XR formulation) or oral solution for the duration noted if the patient meets ONE of the following (A or B):
Note: This includes JIA regardless of type of onset and a patient with juvenile spondyloarthropathy/active sacroiliac arthritis. JIA is also referred to as Juvenile Rheumatoid Arthritis.

A) Initial Therapy. Approve for 6 months if the patient meets the following criteria (i and ii):

i. Patient meets ONE of the following (a or b):

a) Patient has had a 3-month trial of at least one tumor necrosis factor inhibitor; OR

b) Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND
Note: Refer to Appendix for examples of tumor necrosis factor inhibitors. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.

ii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Xeljanz. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xeljanz is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Xeljanz); OR
Note: Examples of objective measures include Physician Global Assessment (MD global), Parent/Patient Global Assessment of Overall Well-Being (PGA), Parent/Patient Global Assessment of Disease Activity (PDA), Juvenile Arthritis Disease Activity Score (JDAS), Clinical Juvenile Arthritis Disease Activity Score (cJDAS), Juvenile Spondyloarthritis Disease Activity Index (JSpADA), serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.

b) Compared with baseline (prior to initiating Xeljanz), patient experienced an improvement in at least one symptom, such as improvement in limitation of motion, less joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living.

3. Psoriatic Arthritis. Approve Xeljanz/Xeljanz XR tablets (not oral solution) for the duration noted if the patient meets ONE of the following criteria (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has had a 3-month trial of at least ONE tumor necrosis factor inhibitor ; OR
  - **b)** Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND

    Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for psoriatic arthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.
- **iii.** The medication will be used in combination with methotrexate or another conventional synthetic disease-modifying antirheumatic drug (DMARD), unless contraindicated; AND

  Note: Examples of other conventional synthetic DMARDs include leflunomide and sulfasalazine.
- **iv.** The medication is prescribed by or in consultation with a rheumatologist or a dermatologist.

B) Patient is Currently Receiving Xeljanz/Xeljanz XR. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient has been established on therapy for at least 6 months; AND

  Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xeljanz/Xeljanz XR is reviewed under criterion A (Initial Therapy).
- **ii.** The medication will be used in combination with methotrexate or another conventional synthetic disease-modifying antirheumatic drug (DMARD), unless contraindicated; AND

  Note: Examples of other conventional synthetic DMARDs include leflunomide and sulfasalazine.
- **iii.** Patient meets at least one of the following (a or b):
  - **a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Xeljanz/Xeljanz XR); OR

    Note: Examples of standardized measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).
  - **c)** Compared with baseline (prior to initiating Xeljanz/Xeljanz XR), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

4. Rheumatoid Arthritis. Approve Xeljanz/Xeljanz XR tablets (not oral solution) for the duration noted if the patient meets ONE of the following criteria (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has had a 3-month trial of at least ONE tumor necrosis factor inhibitor; OR
  - **b)** Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND

    Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for rheumatoid arthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.

iii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Xeljanz/Xeljanz XR. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xeljanz/Xeljanz XR is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR
Note: Examples of objective measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).

b) Patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

5. Ulcerative Colitis. Approve Xeljanz/Xeljanz XR tablets (not oral solution) for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient meets ONE of the following (a or b):

a) Patient has had a 3-month trial of at least ONE tumor necrosis factor inhibitor; OR

b) Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND
Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for ulcerative colitis.

iii. The medication is prescribed by or in consultation with a gastroenterologist.

B) Patient is Currently Receiving Xeljanz/Xeljanz XR. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with Xeljanz/Xeljanz XR is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Xeljanz/Xeljanz XR); OR
Note: Examples of objective measures include fecal markers (e.g., fecal calprotectin), serum markers (e.g., C-reactive protein), endoscopic assessment, and/or reduced dose of corticosteroids.

b) Compared with baseline (prior to initiating Xeljanz/Xeljanz XR), patient experienced an improvement in at least one symptom, such as decreased pain, fatigue, stool frequency, and/or decreased rectal bleeding.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Xeljanz/Xeljanz XR is not recommended in the following situations:

1. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (DMARD).** Xeljanz/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/Xeljanz XR with a targeted synthetic DMARD; therefore, safety and efficacy of these combinations are unknown.

2. **Concurrent use with Other Potent Immunosuppressants** (e.g., azathioprine, tacrolimus, cyclosporine, mycophenolate mofetil).[1] Co-administration with other potent immunosuppressive drugs has the risk of added immunosuppression and has not been evaluated in rheumatoid arthritis. In ulcerative colitis, Xeljanz is not recommended for use in combination with potent immunosuppressants such as azathioprine and cyclosporine.
   Note: This does NOT exclude use of Xeljanz/Xeljanz XR with methotrexate for rheumatoid arthritis; Xeljanz/Xeljanz XR has been evaluated in patients with rheumatoid arthritis taking background methotrexate, leflunomide, or combinations of disease-modifying antirheumatic drugs (DMARDs) containing methotrexate and/or leflunomide.

3. **COVID-19 (Coronavirus Disease 2019).** Forward all requests to the Medical Director.
   Note: This includes requests for cytokine release syndrome associated with COVID-19.

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.[7] However, based on Phase IIb studies, there are concerns of Epstein Barr Virus-associated post-transplant lymphoproliferative disorder in certain transplant patients receiving Xeljanz.[1,6]

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Xeljanz®/Xeljanz XR [prescribing information]. New York, NY: Pfizer; December 2021.
2. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis Rheum*. 2013;65(10):2499-2512.
3. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2019;71(1):2-29.
4. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123.
5. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
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7. 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.
8. Ward MM, Deodhar A, Gensler LS, et al. 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2019;71(10):1599-1613.

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Juvenile Idiopathic Arthritis:** The approval condition was reworded to as listed. Previously the indication also included Juvenile Rheumatoid Arthritis (regardless of type of onset), which was moved into a Note.	08/04/2021
Selected Revision	**Juvenile Idiopathic Arthritis:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving, it was clarified that this applies to a patient who is receiving Xeljanz for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years. **Psoriatic Arthritis:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving, it was clarified that this applies to a patient who is receiving Xeljanz/Xeljanz XR for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years. **Rheumatoid Arthritis:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving, it was clarified that this applies to a patient who is receiving Xeljanz/Xeljanz XR for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years. **Ulcerative Colitis:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving, it was clarified that this applies to a patient who is receiving Xeljanz/Xeljanz XR for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years.	12/01/2021
Selected Revision	**Ankylosing Spondylitis:** This newly approved indication was added to the policy. **Juvenile Idiopathic Arthritis:** To align with the updated labeling, the requirement for a previous therapy prior to Xeljanz was changed from a 3-month trial of one other therapy to a 3-month trial of at least one tumor necrosis factor inhibitor (TNFi). An exception for a patient who has tried a TNFi but could not tolerate a 3-month trial was also added. The exception for a patient with aggressive disease, as determined by the prescriber, was removed. **Psoriatic Arthritis:** To align with the updated labeling, the requirement for a previous therapy prior to Xeljanz/Xeljanz XR was changed from a 3-month trial of a conventional synthetic disease modifying drug to a 3-month trial of at least one TNFi. An exception for a patient who has tried a TNFi but could not tolerate a 3-month trial was also added. **Rheumatoid Arthritis:** To align with the updated labeling, the requirement for a previous therapy prior to Rinvoq was changed from a 3-month trial of a conventional synthetic disease modifying drug to a 3-month trial of at least one TNFi. An exception for a patient who has tried a TNFi but could not tolerate a 3-month trial was also added. **Ulcerative Colitis:** The requirement for a trial of at least one TNFi was changed to specify that the trial was for at least 3-months (previously no duration was specified). An exception for a patient who has tried a TNFi but could not tolerate a 3-month trial was also added.	12/15/2021
Annual Revision	No criteria changes.	08/31/2022

APPENDIX

* Not an all-inclusive list of indications (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis.