PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 07/15/2020

OVERVIEW

Xeljanz/Xeljanz XR is an inhibitor of the Janus kinases (JAK) pathways approved for the following uses:[1]

- **Psoriatic arthritis**, for treatment of patients who have had an inadequate response or intolerance to methotrexate or other disease-modifying antirheumatic drugs (DMARDs). In psoriatic arthritis, Xeljanz/XR should be used in combination with a conventional synthetic DMARD.
- **Rheumatoid arthritis**, for treatment of adults with moderately to severely active disease who have had an inadequate response or intolerance to methotrexate, either as monotherapy or in combination with methotrexate or other nonbiologic DMARDs.
- **Ulcerative colitis**, for treatment of adults with moderately to severely active disease who have had an inadequate response or who are intolerant to tumor necrosis factor inhibitors (TNFis).

Safety and efficacy have not been established in patients < 18 years of age. For all indications, Xeljanz/XR is not recommended for use in combination with biologics or potent immunosuppressants such as azathioprine or cyclosporine.

Guidelines

Guidelines for treatment of inflammatory conditions recommend assessment of response to initial therapy, most often within 3 months of initiating or changing therapy. In ulcerative colitis, the Prescribing Information recommends discontinuation of Xeljanz/XR if adequate therapeutic response is not achieved by Week 16.

- **Psoriatic Arthritis:** Guidelines from American College of Rheumatology (ACR) [2019] 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.[2]
- **Rheumatoid Arthritis:** Guidelines from ACR (2015) have TNFis and non-TNF biologics, administered with or without methotrexate, equally positioned as a recommended therapy following a trial of a conventional synthetic DMARD (e.g., methotrexate, leflunomide, hydroxychloroquine, sulfasalazine).[3]
- **Ulcerative Colitis:** Guidelines from the American College of Gastroenterology for UC (2019) note that the following agents can be used for induction of remission in moderately to severely active disease: Uceris tablets; Oral or intravenous systemic corticosteroids Entyvio, Xeljanz, or TNFis (adalimumab, Simponi SC, infliximab).[4] Guidelines from the American Gastroenterological Association (2020) recommend Xeljanz only after failure of or intolerance to a TNFi.[5]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Xeljanz/Xeljanz XR. Because of the specialized skills required for evaluation and diagnosis of patients treated with Xeljanz as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Xeljanz/Xeljanz XR to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

All reviews for use of 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 the following criteria:

FDA-Approved Indications

1. **Psoriatic Arthritis.** Approve for the duration noted if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND
       Note: Examples include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic. Refer to Appendix for examples of biologics used for psoriatic arthritis. These patients who have already tried a biologic are not required to "step back" and try a conventional synthetic DMARD).
     - **iii.** The medication will be used concomitantly with methotrexate or another conventional synthetic DMARD, unless contraindicated; AND
       Note: Examples of other conventional synthetic DMARDs include leflunomide and sulfasalazine.
     - **iv.** The agent is prescribed by or in consultation with a rheumatologist or a dermatologist.
   - **B)** Patient is Currently Receiving Xeljanz/XR. Approve for 3 years if the patient meets BOTH of the following (i and ii):
     - **i.** The medication will be used concomitantly with methotrexate or another conventional synthetic DMARD, unless contraindicated; AND
       Note: Examples of other conventional synthetic DMARDs include leflunomide and sulfasalazine.
     - **ii.** The patient has responded as determined by the prescriber.
       Note: Examples of a response to therapy include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants (for example, C-reactive protein). The patient may not have a full response, but there should have been a recent or past response to Xeljanz/XR.

2. **Rheumatoid Arthritis.** Approve for the duration noted if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND

Note: Examples include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic. Refer to Appendix for examples of biologics used for rheumatoid arthritis. These patients who have already tried a biologic are not required to "step back" and try a conventional synthetic DMARD).

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

B) Patient is Currently Receiving Xeljanz/Xeljanz XR. Approve for 3 years if the patient has had a response, as determined by the prescriber.

Note: Examples of a response to therapy include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids. The patient may not have a full response, but there should have been a recent or past response to Xeljanz/Xeljanz XR.

3. **Ulcerative Colitis.** Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient has had a trial of at least ONE tumor necrosis factor inhibitor for ulcerative colitis; AND

Note: Examples of a tumor necrosis factor inhibitor include an adalimumab product, an infliximab product, Simponi SC (golimumab SC injection).

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

B) Patient is Currently Receiving Xeljanz/XR. Approve for 3 years if the patient has had a response, as determined by the prescriber.

Note: Examples of a response include decreased stool frequency or rectal bleeding. The patient may not have a full response, but there should have been a recent or past response to Xeljanz/XR.

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 DMARD.** Xeljanz/XR should not be administered in combination with a biologic used for an inflammatory condition (see Appendix for examples).[1] Combination therapy is generally not recommended due to a potential for a higher rate of adverse effects with combinations and lack of evidence supporting additive efficacy.[7-8] There are no data evaluating combination of Xeljanz/XR with a targeted synthetic DMARD (e.g., Otezla); therefore, safety and efficacy of this combination is unknown.

2. **Concurrent use with Other Potent Immunosuppressants** (e.g., azathioprine, tacrolimus, cyclosporine, mycophenolate mofetil).[1] Coadministration with other potent immunosuppressive drugs has the risk of added immunosuppression and has not been evaluated in RA. In UC, 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 MTX for RA; Xeljanz/Xeljanz XR has been evaluated in patients with RA taking background MTX, leflunomide, or combinations of DMARDs containing MTX 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.[9] However, based on Phase IIb studies, there are concerns of Epstein Barr Virus-associated post-transplant lymphoproliferative disorder (PTLD) in certain transplant patients receiving Xeljanz.[1,6]

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 tablets/extended release tablets [prescribing information]. New York, NY: Pfizer Inc; December 2019.
2. 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.
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
4. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
5. Feuerstein JD, Isaac s KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158:1450-1461.
6. 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.

APPENDIX

Biologic	Mechanism of Action	Examples of Inflammatory Indications for Products*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzza SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indication (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; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; 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; ^ Off-label use of Kineret in JIA supported in guidelines; DMARDs – Disease-modifying antirheumatic drug.