Effective Date **6/1/2024**
Coverage Policy Number **IP0230**

Tofacitinib

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for tofacitinib (Xeljanz® tablet, Xeljanz® XR tablet, Xeljanz Oral Solution).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Tofacitinib (Xeljanz, Xeljanz XR, Xeljanz Oral Solution) is considered medically necessary when ONE of the following is met:

1. **Ankylosing spondylitis** [Xeljanz / Xeljanz XR tablets, not oral solution]**.** Individual meets **ALL** of the following:
   A. 18 years of age or older
   B. Documentation of **ONE** of the following:
      i. For Non-axial disease, **ONE** of the following:

a. Failure to **ONE** conventional synthetic disease-modifying anti-rheumatic drug (csDMARD)
b. Contraindication or intolerance to csDMARD therapy

ii. For Axial disease, failure, contraindication, or intolerance to **ONE** nonsteroidal anti-inflammatory drug (NSAID)

iii. Already tried a biologic or targeted synthetic DMARD

C. Documentation of **ONE** of the following:
i. Failure to **ONE** tumor necrosis factor inhibitor (TNFi)
ii. Contraindication or intolerance to TNF inhibitors

D. Medication is being prescribed by, or in consultation with, rheumatologist

E. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

2. **Juvenile Idiopathic Arthritis (JIA) [includes JIA regardless of type of onset and an individual with juvenile spondyloarthropathy/active sacroiliac arthritis. JIA is also referred to as Juvenile Rheumatoid Arthritis.]** [Xeljanz tablets or oral solution, not Xeljanz XR formulation]**.** Individual meets **ALL** of the following criteria:
A. 2 years of age or older
B. Documentation of **ONE** of the following:
i. Failure to **ONE** tumor necrosis factor inhibitor (TNFi)
ii. Contraindication or intolerance to TNF inhibitors
C. Medication is being prescribed by, or in consultation with, a rheumatologist
D. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

3. **Psoriatic Arthritis** [Xeljanz / Xeljanz XR tablets, not oral solution]**.** Individual meets **ALL** of the following criteria:
A. 18 years of age or older
B. Documentation of **ONE** of the following:
i. For Non-axial disease, **ONE** of the following:
a. Failure to **ONE** disease-modifying anti-rheumatic drug (DMARD)
b. Contraindication or intolerance to **ALL** disease-modifying anti-rheumatic drug (DMARD) therapy
ii. For Axial disease, **ONE** of the following:
a. Failure to **ONE** disease-modifying anti-rheumatic drug (DMARD), OR a nonsteroidal anti-inflammatory drug (NSAID)
b. Contraindication or intolerance to **ALL** disease-modifying anti-rheumatic drug (DMARD) therapy AND nonsteroidal anti-inflammatory drugs (NSAIDs)
iii. Already tried a biologic or targeted synthetic DMARD
C. Documentation of **ONE** of the following:
i. Failure to **ONE** tumor necrosis factor inhibitor (TNFi)
ii. Contraindication or intolerance to TNF inhibitors
D. Medication will be used in combination with standard first-line therapy (i.e. csDMARD, or NSAID), unless contraindicated
E. Medication is being prescribed by, or in consultation with, a rheumatologist or dermatologist
F. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

4. **Rheumatoid Arthritis** [Xeljanz / Xeljanz XR tablets, not oral solution]**.** Individual meets **ALL** of the following criteria:
A. 18 years of age or older
B. Documentation of **ONE** of the following:
i. Failure after 3 months to **ONE** conventional synthetic disease-modifying anti-rheumatic drug (csDMARD)
ii. Contraindication or intolerance to **ALL** csDMARD

iii. Already tried a biologic or target synthetic DMARD

C. Documentation of **ONE** of the following:
   i. Failure after 3 months to **ONE** tumor necrosis factor inhibitor (TNFi)
   ii. Contraindication or intolerance to TNF inhibitors
D. Medication is being prescribed by, or in consultation with, a rheumatologist
E. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

5. **Ulcerative Colitis** [Xeljanz / Xeljanz XR tablets, not oral solution]**.** Individual meets **BOTH** of the following criteria:
   A. 18 years of age or older
   B. Medication is being prescribed by, or in consultation with, a gastroenterologist
   C. Preferred Product Step Therapy Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plans]

Coverage varies across plans and requires the use of preferred products. Refer to the customer's benefit plan document for coverage details.

Employer Group Plans	
Condition	**Preferred Product Step Therapy Criteria**
Ankylosing Spondylitis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/ Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Juvenile Idiopathic Arthritis [Xeljanz tablet, oral solution]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/ Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Psoriatic Arthritis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/ Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Rheumatoid Arthritis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **adalimumab – adbm/ Cyltezo**, **adalimumab-ryvk/ Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Ulcerative Colitis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following **adalimumab products:** A. **Adalimumab-adaz or Hyrimoz** (by Sandoz) [requires prior authorization] B. **Adalimumab - adbm or Cyltezo** [requires prior authorization] C. **Adalimumab-ryvk** or **Simlandi** [requires prior authorization] D. **Humira** (by AbbVie) [requires prior authorization]

Individual and Family Plan	
Condition	**Preferred Product Step Therapy Criteria**
Ankylosing Spondylitis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Juvenile Idiopathic Arthritis [Xeljanz tablet, oral solution]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Psoriatic Arthritis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Rheumatoid Arthritis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following: A. **Adalimumab Product** (**adalimumab-adaz/Hyrimoz** [by Sandoz/Novartis], **Adalimumab – adbm/Cyltezo**, **adalimumab-ryvk/Simlandi**, or **Humira** [by AbbVie]) [requires prior authorization] B. **Enbrel** [requires prior authorization]
Ulcerative Colitis [Xeljanz / XR tablet]	Documentation of failure, contraindication, or intolerance to **ONE** of the following adalimumab products**:** A. **Adalimumab-adaz** or **Hyrimoz** (by Sandoz/Novartis) [requires prior authorization] B. **Adalimumab - adbm** or **Cyltezo** [requires prior authorization] C. **Adalimumab-ryvk** or **Simlandi** [requires prior authorization] D. **Humira** (by AbbVie) [requires prior authorization]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of tofacitinib (Xeljanz/Xeljanz XR) is considered medically necessary for **ALL** covered diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven including the following (this list may not be all inclusive):

1. **Alopecia.** Insufficient efficacy and safety data to support use in alopecia. Xeljanz is not indicated for this use.[1]

2. **Atopic Dermatitis.** Insufficient efficacy and safety data to support use in atopic dermatitis. Xeljanz is not indicated for this use.[1]

3. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (tsDMARD).** 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 Rinvoq with other targeted synthetic DMARDs; therefore, safety and efficacy of these combinations are unknown.

4. **COVID-19 (Coronavirus Disease 2019).** This includes requests for cytokine release syndrome associated with COVID-19.

5. **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]

6. **Vitiligo.** Insufficient efficacy and safety data to support use in vitiligo. Xeljanz is not indicated for this use.[1] A small case series of 10 individuals with vitiligo were treated with JAK inhibitors. Five subjects achieved some repigmentation at sites of either sunlight exposure or low dose nbUVB light. The authors stated that JAK monotherapy does not seem to be effective, but appears to need concurrent nbUVB phototherapy or sunlight exposure. The authors concluded that prospective clinical trials are necessary to evaluate the use of JAK inhibitors in vitiligo. This study was limited by small sample size, retrospective design and no control group.[9]

Background

OVERVIEW
Xeljanz/Xeljanz XR is an inhibitor of the Janus kinases pathways.[1] 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 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/Xeljanz XR if adequate therapeutic response is not achieved by Week 16.

- **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 IL-17 blockers are recommended over 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, enthesitis. Actemra® (tocilizumab intravenous, tocilizumab subcutaneous) and Orencia® (abatacept intravenous, abatacept subcutaneous) 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 [NSAID] 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]

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.
6. 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.
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.
9. Liu LY, Strassner JP, Refat MA, et al. Repigmentation in vitiligo using the janus kinase inhibitor, tofacitinib, may require concomitant light exposure. J Am Acad Dermatol. 2017 October ; 77(4): 675–682.

APPENDIX

Table 1. Approved TNFis for Targeted Indications.

	Rheumatology					Dermatology	Gastroenterology	
	RA	JIA	AS	nr-axSpA	PsA	PsO	CD	UC
Tumor Necrosis Factor Inhibitors								
Cimzia	√	--	√	√	√	√	√	--
Enbrel	√	√	√	--	√	√	--	--
Adalimumab products (Humira, biosimilars)	√	√	√	--	√	√	√	√
Infliximab Products	√	--	√	--	√	√	√	√
Simponi Subcutaneous	√	--	√	--	√	--	--	√
Simponi Aria	√	√	√	--	√	--	--	--

TNFis – Tumor necrosis factor inhibitors; RA – Rheumatoid arthritis; JIA – Juvenile idiopathic arthritis; AS – Ankylosing spondylitis; nr-axSpA – Non-radiographic spondyloarthritis; PsA – Psoriatic arthritis; PsO – Plaque psoriasis; CD – Crohn's disease; UC – Ulcerative colitis.

Table 2. Approved IL-17, IL-23, and IL-12/23 Blockers for Targeted Indications.

	Rheumatology			Dermatology	Gastroenterology	
	Ankylosing Spondylitis	nr-axSpA	Psoriatic Arthritis	Plaque Psoriasis	Crohn's Disease	Ulcerative Colitis
Interleukin-17 Blockers						
Cosentyx	√	√	√	√	--	--
Siliq	--	--	--	√	--	--
Taltz	√	√	√	√	--	--
Interleukin-23 Blockers						
Ilumya	--	--	--	√	√	--
Skyrizi Intravenous	--	--	--	--	√#	--
Skyrizi Subcutaneous	--	--	√	√	√^	--
Tremfya	--	--	√	√	--	--
Interleukin-12/23 Blockers						
Stelara Subcutaneous	--	--	√	√	√^	√^
Stelara Intravenous	--	--	--	--	√#	√#

IL – Interleukin; nr-axSpA – Non-radiographic spondyloarthritis; ^ Maintenance dosing only; # Induction dosing only

Table 3. Approved tsDMARDs for Targeted Indications.

	Rheumatology					Dermatology	Gastro-enterology
	Rheumatoid Arthritis	Juvenile Idiopathic Arthritis	Ankylosing Spondylitis	nr-axSpA	Psoriatic Arthritis	Plaque Psoriasis	Ulcerative Colitis
Janus Kinases Inhibitors							
Olumiant	√	--	--	--	--	--	--
Opzelura	--	--	--	--	--	--	--
Rinvoq	√	--	√	√	√	--	√

	Rheumatology					Dermatology	Gastro-enterology
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Ankylosing Spondylitis**	**nr-axSpA**	**Psoriatic Arthritis**	**Plaque Psoriasis**	**Ulcerative Colitis**
Xeljanz tablets	√	√[#]	√	--	√	--	√
Xeljanz oral solution	--	√[#]	--	--	--	--	--
Xeljanz XR	√	--	√	--	√	--	√
Phosphodiesterase Type 4 Inhibitor							
Otezla	--	--	--	--	√	√	--
Sphingosine 1-Phosphate Receptor Modulator							
Zeposia	--	--	--	--	--	--	√
Tyrosine Kinase 2 Inhibitor							
Sotyktu	--	--	--	--	--	√	--

tsDMARDs – Targeted synthetic disease-modifying antirheumatic drugs; [#] Indicated in polyarticular JIA.

Table 4. Other Approved Biologics for Targeted Indications.

	Rheumatology		
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Psoriatic Arthritis**
Interleukin-6 Blockers			
Actemra Intravenous	√	√[^]	--
Actemra Subcutaneous	√	√[^]	--
Kevzara	√	--	--
Interleukin-1 Blocker			
Kineret	√	--	--
T-Cell Costimulation Modulator			
Orencia Intravenous	√	√[#]	√
Orencia Subcutaneous	√	√[#]	√
CD20-Directed Cytolytic Antibody			
Rituximab Intravenous Products	√	--	--

^ Indicated in polyarticular and systemic JIA; [#] Indicated in polyarticular JIA.