

Clinical Policy: Tofacitinib (Xeljanz, Xeljanz XR)

Reference Number: CP.PHAR.267

Effective Date: 01.30.18

Last Review Date: 05.20

Line of Business: Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Tofacitinib (Xeljanz[®], Xeljanz[®] XR) is a Janus kinase (JAK) inhibitor.

FDA Approved Indication(s)

Xeljanz and Xeljanz XR are indicated for the treatment of:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate (MTX). They may be used as monotherapy or in combination with MTX or other nonbiologic disease-modifying antirheumatic drugs (DMARDs).
- Adult patients with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to MTX or other DMARDs.
- Adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response or who are intolerant to TNF blockers.

Limitation(s) of use: Use of Xeljanz/Xeljanz XR in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Xeljanz and Xeljanz XR are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Rheumatoid Arthritis (must meet all):

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (*see Appendix F*);
2. Prescribed by or in consultation with a rheumatologist;
3. Age \geq 18 years;
4. Member meets one of the following (a or b):
 - a. Failure of a \geq 3 consecutive month trial of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
 - b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a \geq 3 consecutive month trial of at least ONE conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated

doses, unless contraindicated or clinically significant adverse effects are experienced;

5. Documentation of baseline clinical disease activity index (CDAI) score (*see Appendix G*);
6. Dose does not exceed one of the following (a or b):
 - a. Xeljanz: 10 mg (2 tablets) per day;
 - b. Xeljanz XR: 11 mg (1 tablet) per day.

Approval duration: 6 months

B. Psoriatic Arthritis (must meet all):

1. Diagnosis of PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age \geq 18 years;
4. Dose does not exceed one of the following (a or b):
 - a. Xeljanz: 10 mg (2 tablets) per day;
 - b. Xeljanz XR: 11 mg (1 tablet) per day.

Approval duration: 6 months

C. Ulcerative Colitis (must meet all):

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age \geq 18 years;
4. Documentation of a Mayo Score \geq 6 (*see Appendix E*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed one of the following (a or b):
 - a. Xeljanz: 20 mg (2 tablets) per day;
 - b. Xeljanz XR: 22 mg (1 tablet) per day.

Approval duration: 6 months

D. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
 - a. For RA member is responding positively to therapy as evidenced by a decrease in CDAI score since baseline (*see Appendix G*);
 - b. For all other indications: member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
 - a. Xeljanz (i or ii):

- i. RA or PsA: 10 mg (2 tablets) per day;
- ii. UC: 20 mg (2 tablets) per day;
- b. Xeljanz XR (i or ii):
 - i. RA or PsA: 11 mg (1 tablet) per day;
 - ii. UC: 22 mg (1 tablet) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DMARDs: disease-modifying antirheumatic drugs	MTX: methotrexate
FDA: Food and Drug Administration	RA: rheumatoid arthritis
JAK: Janus kinase	PsA: psoriatic arthritis
	UC: ulcerative colitis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan [®] , Imuran [®])	RA 1 mg/kg/day PO QD or divided BID	2.5 mg/kg/day
Cuprimine [®] (d-penicillamine)	RA* <u>Initial dose:</u> 125 or 250 mg PO QD <u>Maintenance dose:</u> 500 – 750 mg/day PO QD	1,500 mg/day
cyclosporine (Sandimmune [®] , Neoral [®])	RA 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
hydroxychloroquine (Plaquenil [®])	RA* <u>Initial dose:</u> 400 – 600 mg/day PO QD	600 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<u>Maintenance dose:</u> 200 – 400 mg/day PO QD	
leflunomide (Arava [®])	RA 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
methotrexate (Rheumatrex [®])	RA 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
Ridaura [®] (auranofin)	RA 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine [®])	RA 2 g/day PO in divided doses	RA: 3 g/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
 - Serious infections: There is an increased risk of serious infections leading to hospitalization or death.
 - Mortality: Rheumatoid arthritis patients 50 years and older with at least one cardiovascular risk factor treated with Xeljanz 10 twice daily had a higher rate of all-cause mortality, including sudden CF death, compared to those treated with Xeljanz 5 mg given twice daily or TNF blockers in a large, ongoing, post marketing study.
 - Malignancies: Lymphoma and other malignancies, as well as Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed.
 - Thrombosis: Thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis have occurred in patients treated with Xeljanz and other Janus kinase inhibitors used to treat inflammatory conditions.
 - A large, ongoing postmarketing safety study observed an increase in incidence of thrombosis events in rheumatoid arthritis patients who were 50 years of age and older with at least one CV risk factor treated with Xeljanz 10 mg twice daily compared to Xeljanz 5 mg twice daily or TNF blockers.

Appendix D: General Information

- Definition of failure of MTX or DMARDs
 - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
 - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so

- patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to therapy may include, but are not limited to:
 - Reduction in joint pain/swelling/tenderness
 - Improvement in erythrocyte sedimentation rates/C-reactive protein (ESR/CRP) levels
 - Improvements in activities of daily living
 - Only the immediate-release version of Xeljanz is FDA-approved for the treatment of UC.
 - PsA: According to the 2018 American College of Rheumatology and National Psoriasis Foundation guidelines, TNF inhibitors or oral small molecules (e.g., methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilast) are preferred over other biologics (e.g., interleukin-17 inhibitors or interleukin-12/23 inhibitors) for treatment-naïve disease. TNF inhibitors are also generally recommended over oral small molecules as first-line therapy unless disease is not severe, member prefers oral agents, or TNF inhibitor therapy is contraindicated.

Appendix E: Mayo Score

- Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician’s global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0 – 2	Remission
3 – 5	Mild activity
6 – 10	Moderate activity
>10	Severe activity

- The following may be considered for medical justification supporting inability to use an immunomodulator for ulcerative colitis:
 - Documentation of Mayo Score 6 – 12 indicative of moderate to severe ulcerative colitis.

Appendix F: The 2010 ACR Classification Criteria for RA

Add score of categories A through D; a score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	Joint involvement	Score
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5

B	Serology (at least one test result is needed for classification)	
	Negative rheumatoid factor (RF) <i>and</i> negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF <i>or</i> low positive ACPA <i>* Low: < 3 x upper limit of normal</i>	2
	High positive RF <i>or</i> high positive ACPA <i>* High: ≥ 3 x upper limit of normal</i>	3
C	Acute phase reactants (at least one test result is needed for classification)	
	Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
	Abnormal CRP or normal ESR	1
D	Duration of symptoms	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix G: Clinical Disease Activity Index (CDAI) Score

The Clinical Disease Activity Index (CDAI) is a composite index for assessing disease activity in RA. CDAI is based on the simple summation of the count of swollen/tender joint count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity. The CDAI score ranges from 0 to 76.

CDAI Score	Disease state interpretation
≤ 2.8	Remission
2.8 to ≤ 10	Low disease activity
10 to ≤ 22	Moderate disease activity
> 22	High disease activity

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Tofacitinib immediate-release (Xeljanz)	PsA	5 mg PO BID	10 mg/day
	RA		
	UC	<u>Induction:</u> 10 mg PO BID for 8 weeks, up to 16 weeks <u>Maintenance:</u> 5 mg PO BID	Induction: 20 mg/day Maintenance: 10 mg/day
Tofacitinib extended-release (Xeljanz XR)	PsA	11 mg PO QD	11 mg/day
	RA		
	UC	<u>Induction:</u> 22 mg PO QD for 8 weeks, up to 16 weeks <u>Maintenance:</u> 11 mg PO QD	Induction: 22 mg/day Maintenance: 11 mg/day

VI. Product Availability

Drug Name	Availability
Tofacitinib immediate- release (Xeljanz)	Tablets: 5 mg, 10 mg
Tofacitinib extended-release (Xeljanz XR)	Tablets: 11 mg, 22 mg

VII. References

1. Xeljanz/Xeljanz XR Prescribing Information. New York, NY: Pfizer Labs; December 2019. Available at: www.xeljanz.com. Accessed February 28, 2020.
2. Singh JA, Furst DE, Bharat A, et al. 2012 Update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res.* 2012;64(5):625-639.
3. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Rheumatology* 2016. 68(1):1-26.
4. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis* 2015;0:1-12. doi:10.1136/annrheumdis-2015-208337
5. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *American College of Rheumatology.* 2019; 71(1):5-32. doi: 10.1002/art.40726.
6. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol* 2019;114:384-413

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>Medicaid: Policy split from CP.PHAR.86 Rheumatoid & Juvenile Arthritis & Ankylosing Spondylitis Treatments. Policy converted to new template.</p> <p>Removed contraindications of HBV and malignant disease; added dosign requirements; modified criteria to require trial of methotrexate, unless contraindicated; added sulfasalazine as an alternative to MTX if MTX is contraindicated; added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated; Added the XR formulation to policy.</p> <p>Re-auth: added dosing and reasons to discontinue.</p> <p>Modified approval duration to 6 months for initial and 12 months for renewal; Updated reasons for discontinuation to contraindications and warning and precautions when initiating treatment should be avoided per PI.</p>	06.16	07.16
<p>Medicaid: Converted to new template. Revised criteria for confirmation of RA diagnosis per 2010 ACR Criteria. Removed safety requirements per updated CPAC Safety Precaution in PA Policies approach.</p>	07.17	07.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: criteria added for new FDA indication: psoriatic arthritis; added HIM; removed TB testing requirement for RA; references reviewed and updated.	02.27.18	05.18
Criteria added for new indication: ulcerative colitis; allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.	07.17.18	02.19
2Q 2019 annual review: removed trial and failure requirement of conventional DMARDs (e.g., MTX)/NSAIDs for PsA per 2018 PsA guidelines; revised GI specialist to gastroenterologist for UC; updated policy to reflect Xeljanz XR is formulary; references reviewed and updated.	03.05.19	05.19
Removed redirection to Humira and/or Enbrel per SDC and prior approved clinical guidance.	04.23.19	
Removed HIM line of business per SDC decision.	12.23.19	
2Q 2020 annual review: for RA, added specific diagnostic criteria for definite RA, baseline CDAI score requirement, and decrease in CDAI score as positive response to therapy; for UC, removed requirement for immediate-release formulation, removed redirection to ASA, 6-MP, AZA, added requirement for Mayo score of at least 6, added a trial of corticosteroids; references reviewed and updated.	04.23.20	05.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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