

## **Clinical Policy: Tofacitinib (Xeljanz, Xeljanz XR)**

Reference Number: CP.PHAR.267

Effective Date: 01.30.18

Last Review Date: 05.19

Line of Business: HIM, Medicaid

[Revision Log](#)

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

### **Description**

Tofacitinib (Xeljanz<sup>®</sup>, Xeljanz<sup>®</sup> XR) is a Janus kinase (JAK) inhibitor.

### **FDA Approved Indication(s)**

Xeljanz is indicated for the treatment of:

- Adult patients with moderately to severely active ulcerative colitis (UC).

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.

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<sup>®</sup> 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;
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. Dose does not exceed one of the following (a or b):
  - a. Xeljanz: 10 mg per day;
  - b. Xeljanz XR: 11 mg 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 per day;
  - b. Xeljanz XR: 11 mg per day.

**Approval duration: 6 months**

**C. Ulcerative Colitis (must meet all):**

1. Diagnosis of UC;
2. Request is for Xeljanz immediate-release;
3. Prescribed by or in consultation with a gastroenterologist;
4. Age  $\geq$  18 years;
5. Failure of a  $\geq$  3 consecutive month trial of azathioprine, 6-mercaptopurine, or aminosalicylate (e.g., sulfasalazine), at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 20 mg 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): HIM.PHAR.21 for health insurance marketplace and 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 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 per day;
    - ii. UC: 20 mg per day;
  - b. Xeljanz XR: 11 mg 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): HIM.PHAR.21 for health insurance marketplace and 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 – HIM.PHAR.21 for health insurance marketplace and 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 <sup>®</sup> , Imuran <sup>®</sup> )	<b>RA</b> 1 mg/kg/day PO QD or divided BID  <b>UC</b> 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
Cuprimine <sup>®</sup> (d-penicillamine)	<b>RA*</b> <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 <sup>®</sup> , Neoral <sup>®</sup> )	<b>RA</b> 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
hydroxychloroquine (Plaquenil <sup>®</sup> )	<b>RA*</b> <u>Initial dose:</u> 400 – 600 mg/day PO QD <u>Maintenance dose:</u> 200 – 400 mg/day PO QD	600 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
leflunomide (Arava <sup>®</sup> )	<b>RA</b> 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
6-mercaptopurine (Purixan <sup>®</sup> )	<b>UC</b> 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
mesalamine (e.g., Pentasa <sup>®</sup> , Asacol <sup>®</sup> , Lialda <sup>®</sup> , etc. )	<b>UC</b> <i>Refer to prescribing information</i>	<i>Refer to prescribing information</i>
methotrexate (Rheumatrex <sup>®</sup> )	<b>RA</b> 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
Ridaura <sup>®</sup> (auranofin)	<b>RA</b> 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine <sup>®</sup> )	<b>RA</b> 2 g/day PO in divided doses  <b>UC</b> <u>Initial dose:</u> <i>Adults:</i> 3 – 4 g/day PO in divided doses (not to exceed Q8 hrs) <i>Pediatrics:</i> 40 – 60 mg/kg/day PO in 3 – 6 divided doses  <u>Maintenance dose:</u> <i>Adults:</i> 2 g PO QD <i>Pediatrics:</i> 30 mg/kg/day PO in 4 divided doses	RA: 3 g/day  UC: 4 g/day

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*\*Off-label*

#### Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - There is an increased risk of serious infections leading to hospitalization or death including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens.
  - Lymphoma and other malignancies have been observed.
  - Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed.

*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.

**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	10 mg PO BID for 8 weeks; then 5 or 10 mg PO BID	20 mg/day
Tofacitinib extended-release (Xeljanz XR)	PsA	11 mg PO QD	11 mg/day
	RA		

**VI. Product Availability**

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

**VII. References**

1. Xeljanz/Xeljanz XR Prescribing Information. New York, NY: Pfizer Labs. October 2018. Available at: [www.xeljanz.com](http://www.xeljanz.com). Accessed February 26, 2019.
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. Van Vollenhoven RF, Fleischmann R, Cohen S, et al. Tofacitinib or adalimumab versus placebo in rheumatoid arthritis. *N Engl J Med.* 2012;367:508-519.
  5. Fleischmann R, Kremer J, Cush J, et al. Placebo-controlled trial of tofacitinib monotherapy in rheumatoid arthritis. *N Engl J Med.* 2012;367:495-507.
  6. Sandborn WJ, Su C, Sands BE, et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. *N Engl J Med.* 2017;376:1723-36.
  7. 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
  8. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>Medicaid: Policy split from CP.PHAR.86 Rheumatoid &amp; Juvenile Arthritis &amp; Ankylosing Spondylitis Treatments. Policy converted to new template.</p> <p>Removed contraindications of HBV and malignant disease; added dosing 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
<p>2Q 2018 annual review: criteria added for new FDA indication: psoriatic arthritis; added HIM; removed TB testing requirement for RA; references reviewed and updated.</p>	02.27.18	05.18
<p>Criteria added for new indication: ulcerative colitis; allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.</p>	07.17.18	02.19
<p>2Q 2019 annual review: removed trial and failure requirement of conventional DMARDs (e.g., MTX)/NSAIDs for PsA per 2018 PsA</p>	03.05.19	05.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
guidelines; revised GI specialist to gastroenterologist for UC; updated policy to reflect Xeljanz XR is formulary; references reviewed and updated.		
Removed redirection to Humira and/or Enbrel per SDC and prior approved clinical guidance.	04.23.19	

**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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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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.

**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy; HIM.PA.103.

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