Clinical Policy: Tofacitinib (Xeljanz, Xeljanz XR)

Reference Number: CP.PHAR.267
Effective Date: 01.30.18
Last Review Date: 02.21
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).
- Adult patients with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to MTX or other disease-modifying antirheumatic drugs (DMARDs).
- Adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response or who are intolerant to tumor necrosis factor (TNF) blockers.

Xeljanz is additionally indicated for active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older.

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. Polyarticular Course Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of pcJIA as evidenced by ≥ 5 joints with active arthritis;
2. Request is for Xeljanz immediate-release tablets or oral solution;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 2 years;
5. Documented baseline 10-point clinical juvenile arthritis disease activity score (cJADAS-10) (*see Appendix I*);
6. Member meets one of the following (a, b, c, or d):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;

b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of leflunomide or sulfasalazine at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
c. For sacroiliitis/axial spine involvement (i.e., spine, hip), failure of a ≥ 4 week trial of an NSAID at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
d. Documented presence of high disease activity as evidenced by cJADAS-10 > 8.5 (*see Appendix I*);

7. Dose does not exceed 10 mg (2 tablets or 10 mL) 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 ≥ 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. 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 ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 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 ≥ 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 one of the following baseline assessment scores (a or b):
   a. Clinical disease activity index (CDAI) score (*see Appendix G*);
   b. Routine assessment of patient index data 3 (RAPID3) score (*see Appendix H)*;
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

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

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;

3. Age ≥ 18 years;
4. Documentation of a Mayo Score ≥ 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

E. 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, b, or c):
   a. For RA: Member is responding positively to therapy as evidenced by one of the following (i or ii):
      i. A decrease in CDAI (*see Appendix G*) or RAPID3 (*see Appendix H*) score from baseline;
      ii. Medical justification stating inability to conduct CDAI re-assessment, and submission of RAPID3 score associated with disease severity that is similar to initial CDAI assessment or improved;
   b. For pcJIA: Member is responding positively to therapy as evidenced by a decrease in cJADAS-10 from baseline (*see Appendix I*);
   c. 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, ii, or iii):
      i. RA or PsA: 10 mg (2 tablets) per day;
      ii. UC: 20 mg (2 tablets) per day;
      iii. pcJIA: 10 mg (2 tablets or 10 mL) 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

CDAI: clinical disease activity index
cJADAS: clinica juvenile arthritis disease activity score
DMARDs: disease-modifying antirheumatic drugs
FDA: Food and Drug Administration
JAK: Janus kinase
MTX: methotrexate
pcJIA: polyarticular course juvenile idiopathic arthritis;
RA: rheumatoid arthritis
RAPID3: routine assessme of patient index data 3
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*** Initial dose: 125 or 250 mg PO QD Maintenance dose: 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*** Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	600 mg/day
leflunomide (Arava®)	**RA** 100 mg PO QD for 3 days, then 20 mg PO QD **PJIA***	20 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Weight < 20 kg: 10 mg every other day Weight 20 - 40 kg: 10 mg/day Weight > 40 kg: 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 **PJIA*** 10 – 20 mg/m^2/week PO, SC, or IM	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 **PJIA*** 30-50 mg/kg/day PO divided BID	RA: 3 g/day PJIA: 2 g/day
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**PJIA*** Varies	Varies

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 patietns 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, indlucing 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 leaste 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

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) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA * *Low: < 3 x upper limit of normal*	2
	High positive RF *or* high positive ACPA * *High: ≥ 3 x upper limit of normal*	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 abnormal 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

Appendix H: Routine Assessment of Patient Index Data 3 (RAPID3) Score
The Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of the three patient-reported ACR core data set measures: function, pain, and patient global estimate of status. Each of the individual measures is scored 0 – 10, and the maximum achievable score is 30.

RAPID3 Score	Disease state interpretation
≤ 3	Remission
3.1 to 6	Low disease activity
6.1 to 12	Moderate disease activity
> 12	High disease activity

Appendix I: Clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS-10)
The cJADAS10 is a continuous disease activity score specific to JIA and consisting of the following three parameters totaling a maximum of 30 points:

- Physician's global assessment of disease activity measured on a 0-10 visual analog scale (VAS), where 0 = no activity and 10 = maximum activity;
- Parent global assessment of well-being measured on a 0-10 VAS, where 0 = very well and 10 = very poor;

- Count of joints with active disease to a maximum count of 10 active joints*

**ACR definition of active joint: presence of swelling (not due to currently inactive synovitis or to bony enlargement) or, if swelling is not present, limitation of motion accompanied by pain, tenderness, or both*

cJADAS-10	Disease state interpretation
≤ 1	Inactive disease
1.1 to 2.5	Low disease activity
2.51 to 8.5	Moderate disease activity
> 8.5	High disease activity

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Tofacitinib immediate-relase (Xeljanz)	pcJIA	• 10 kg ≤ body weight < 20 kg: 3.2 mg (3.2 mL oral solution) PO BID • 20 kg ≤ body weight < 40 kg: 4 mg (4 mL oral solution) PO BID • Body weight ≥ 40 kg: 5 mg PO BID	10 mg/day
	PsA RA	5 mg PO BID	
	UC	Induction: 10 mg PO BID for 8 weeks, up to 16 weeks Maintenance: 5 mg PO BID	Induction: 20 mg/day Maintenance: 10 mg/day
Tofacitinib extended-release (Xeljanz XR)	PsA RA	11 mg PO QD	11 mg/day
	UC	Induction: 22 mg PO QD for 8 weeks, up to 16 weeks Maintenance: 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 Oral solution: 1 mg/mL
Tofacitinib extended-release (Xeljanz XR)	Tablets: 11 mg, 22 mg

VII. References

1. Xeljanz/Xeljanz XR Prescribing Information. New York, NY: Pfizer Labs; September 2020. Available at: www.xeljanz.com. Accessed October 5, 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.
7. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. *Arthritis Care & Res.* 2019; 71(6):717-734. doi: 10.1002/acr.23870.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.	07.17	07.17
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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revised typo in Appendix E from "normal ESR" to "abnormal ESR" for a point gained for ACR Classification Criteria.	11.22.20	
RT2: Added criteria for newly FDA-approved indication for Xeljanz: pcJIA; RT4: updated Xeljanz new dosage form: oral solution; references reviewed and updated. Added criteria for RAPID3 assessment for RA given limited in-person visits during COVID-19 pandemic, updated appendices.	11.17.20	02.21

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.