Clinical Policy: Tofacitinib (Xeljanz/Xeljanz XR)

Reference Number: PA.CP.PHAR.267
Effective Date: 01/18
Last Review Date: 04/19 Revision Log

Description
Tofacitinib (Xeljanz®/Xeljanz® XR) is a Janus kinase (JAK) inhibitor.

FDA approved indication
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 of use: Use of Xeljanz or Xeljanz XR in combination with biologic DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria)

It is the policy of PA Health and Wellness® 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 ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of MTX for ≥ 3 consecutive months 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 sulfasalazine, leflunomide, or hydroxychloroquine for ≥ 3 consecutive months unless at up to maximally indicated doses, contraindicated or clinically significant adverse effects are experienced;
5. Failure of etanercept *(Enbrel is preferred)* AND adalimumab *(Humira is preferred),* each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced, or member is currently receiving Xeljanz;

**Prior authorization is required for etanercept and adalimumab*

6. Dose does not exceed (a or b):
   a. Xeljanz: 10 mg/day;
   b. Xeljanz XR: 11 mg/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. Failure of etanercept *(Enbrel is preferred)* and adalimumab *(Humira is preferred),* each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced, or member is currently receiving Xeljanz;
   **Prior authorization is required for etanercept and adalimumab*
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

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 ≥ 18 years;
5. Failure of a ≥ 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, or member is currently receiving tofacitinib;
6. Failure of a ≥ 3 consecutive month trial of adalimumab *(Humira® is preferred)* unless contraindicated or clinically significant adverse effects are experienced, or member is currently receiving tofacitinib;
   **Prior authorization is required for adalimumab*
7. Dose does not exceed 20 mg per day.

Approval duration: 6 months

D. Other diagnoses/indications

1. Refer to PA.CP.PMN.53.

II. Continued Approval

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

1. Currently receiving medication via PA Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed:
   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 PA Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DMARDs: disease-modifying antirheumatic drugs
FDA: Food and Drug Administration
JAK: Janus kinase
MTX: methotrexate
RA: rheumatoid arthritis
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 **UC** 1.5 – 2 mg/kg/day PO	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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
leflunomide (Arava®)	**RA** 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
6-mercaptopurine (Purixan®)	**UC** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
mesalamine (e.g., Pentasa®, Asacol®, Lialda®, etc.)	**UC** *Refer to prescribing information*	*Refer to prescribing information*
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 **UC** Initial dose: *Adults*: 3 – 4 g/day PO in divided doses (not to exceed Q8 hrs) *Pediatrics*: 40 – 60 mg/kg/day PO in 3 – 6 divided doses Maintenance dose: *Adults*: 2 g PO QD *Pediatrics*: 30 mg/kg/day PO in 4 divided doses	RA: 3 g/day UC: 4 g/day
Enbrel® (etanercept)	**PsA, RA** 25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
Humira® (adalimumab)	**PsA** 40 mg SC every other week **RA** 40 mg SC every other week (may increase to once weekly) **UC** 160 mg SC on day 1, then 80 mg SC on day 15 then 40 mg SC every other week	PsA, UC: 40 mg every other week RA: 40 mg/week

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):
  - 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.

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Tofacitinib immediate-relase (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		

V. Product Availability

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

VI. References

1. Xeljanz/Xeljanz XR Prescribing Information. New York, NY: Pfizer Labs. October 2018. Available at: 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	Approval Date
2Q 2018 annual review: criteria added for new FDA indication: psoriatic arthritis; removed TB testing requirement for RA; references reviewed and updated.	02.27.18	
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.	04.17.19	