Clinical Policy Title:	tofacitinib
Policy Number:	RxA.749
Drug(s) Applied:	Xeljanz®, Xeljanz® XR, Xeljanz® oral solution
Original Policy Date:	04/18/2022
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Tofacitinib (Xeljanz®/Xeljanz® XR, Xeljanz® oral solution) is a Janus kinase (JAK) inhibitor indicated for:

- **Rheumatoid Arthritis:** For the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more TNF blockers.

- **Psoriatic Arthritis:** For the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.

- **Ankylosing Spondylitis:** For the treatment of adult patients with active ankylosing spondylitis who have had an inadequate response or intolerance to one or more TNF blockers.

- **Ulcerative Colitis:** For the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers.

- **Polyarticular Course Juvenile Idiopathic Arthritis:** For the treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more TNF blockers.

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
tofacitinib (Xeljanz®)	PsA RA AS	5 mg orally twice daily PsA: use in combination with nonbiologic disease-modifying antirheumatic drugs RA: monotherapy or use in combination with nonbiologic disease-modifying antirheumatic drugs Patients with moderate to severe Renal impairment and/or moderate Hepatic impairment dosing: reduce to 5 mg orally once daily	10 mg/day

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
	UC	Induction:10 mg orally twice daily for at least 8 weeks, based on therapeutic response, may continue 10 mg twice daily for a maximum of 16 weeks or transition to maintenance dose. Discontinue after 16 weeks of 10 mg twice daily if adequate therapeutic benefit is not achieved Patients with moderate to severe Renal impairment and/or moderate Hepatic impairment dosing: reduce dose to 5 mg orally twice daily Maintenance: 5 mg twice daily; if loss of response on 5 mg twice daily, then use 10 mg twice daily after assessing the benefits and risks and use for the shortest duration; use lowest effective dose to maintain response. Patients with moderate to severe Renal impairment and/or moderate Hepatic impairment dosing: reduce dose to 5 mg orally once daily	20 mg/day
tofacitinib extended release (Xeljanz® XR)	PsA RA AS	11 mg orally once daily Patients with moderate to severe Renal impairment and/or moderate Hepatic impairment dosing: reduce to 5 mg orally once daily immediate release.	11 mg/day
	UC	Induction: 22 mg once daily for at least 8 weeks; may continue 22 mg once daily for a maximum of 16 weeks or transition to maintenance dose. Discontinue therapy if inadequate response achieved after 16 weeks using 22 mg once daily. Patients with moderate to severe Renal impairment and/or moderate Hepatic impairment dosing: reduce to 11 mg orally once daily extended release Maintenance: 11 mg once daily; if loss of response on 11 mg once daily; then use 22 mg once daily for the shortest duration; use lowest effective dose to maintain response. Patients with moderate to severe Renal impairment and/or moderate Hepatic impairment dosing: reduce to 5 mg orally once daily immediate release.	22 mg daily

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
tofacitinib (Xeljanz® / Xeljanz® oral Solution)	pcJIA	5 mg twice daily or weight-based equivalent twice daily: • 10 kg ≤ body weight <20 kg: 3.2 mg (3.2 mL oral solution) twice daily • 20 kg ≤ body weight <40 kg: 4 mg (4 mL oral solution) twice daily • Body weight ≥40 kg: 5 mg (one 5 mg tablet or 5 mL oral solution) twice daily Patients with moderate to severe Renal impairment and/or moderate Hepatic impairment dosing: reduce to once-daily dosing.	5 mg or 5 ml twice daily

Dosage Forms

- Xeljanz® Tablets: 5 mg, 10 mg tofacitinib
- Xeljanz® XR Tablets: 11 mg, 22 mg tofacitinib
- Xeljanz® Oral Solution: 1 mg/mL tofacitinib

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Rheumatoid Arthritis (must meet all)**:**

1. Diagnosis of RA;
2. Request is for Xeljanz® tablets or Xeljanz® XR tablets;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 18 years;
5. Trial and failure of a ≥ 3 months of at least one conventional systemic therapy (methotrexate [MTX], sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   *Exception: If one biologic DMARD that is FDA-approved for rheumatoid arthritis has been previously tried, then trial of a conventional systemic agent is not required;
6. Trial and failure of a ≥ 3 months of at least one (1) TNF inhibitor (Cimzia®, Humira®, Simponi®/ Simponi Aria, Enbrel®) , unless contraindicated or clinically significant affects are experienced;
7. Dose does not exceed following (a or b):
   a. For Xeljanz®: 10 mg per day;
   b. For Xeljanz® XR: 11 mg per day.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

B. Psoriatic Arthritis (must meet all)**:**

1. Diagnosis of PsA;
2. Request is for Xeljanz® tablets or Xeljanz® XR tablets;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Age ≥ 18 years;
5. Trial and failure of a ≥ 3 months of at least one (1) TNF inhibitor (Cimzia®, Humira®, Simponi®/ Simponi Aria, Enbrel®) , unless contraindicated or clinically significant affects are experienced;
6. Dose does not exceed following (a or b):
   a. For Xeljanz® 10 mg per day;
   b. For Xeljanz® XR 11 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

C. Ankylosing Spondylitis (must meet all):

1. Diagnosis of active ankylosing spondylitis (AS);
2. Request is for Xeljanz® tablets or Xeljanz® XR tablets;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 18 years;
5. Trial and failure of at least two (2) non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for at ≥ 4 weeks unless contraindicated or clinically significant adverse effects are experienced;
6. Trial and failure of at least two (2) of the following agents: Humira®, Simponi®/ Simponi Aria®, Cimzia®, unless contraindicated or clinically significant adverse effects are experienced;
   *Exception: If a total of two TNF inhibitors (Humira, Cimzia®, Simponi®/ Simponi Aria, Enbrel®) has previously been tried and failed, trial of a third TNF inhibitor is not required.
7. Dose does not exceed following (a or b):
   a. For Xeljanz®: 10 mg per day;
   b. For Xeljanz® XR: 11 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

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

1. Diagnosis of UC;
2. Request is for Xeljanz® tablets or Xeljanz® XR tablets;
3. Prescribed by or in consultation with a gastroenterologist;
4. Age ≥ 18 years;
5. Member meets one of the following (a or b):
   a. Trial and failure of ≥ 3 months of at least one (1) conventional agent (azathioprine, 6-mercaptopurine, aminosalicylate) unless contraindicated or clinically significant adverse effects are experienced;
   b. Trial and failure of corticosteroids (e.g., prednisone, methylprednisolone, budesonide) unless contraindicated or significant adverse effects are experienced;
      *Exception: If one biologic DMARD that is FDA-approved for ulcerative colitis has been previously tried, then trial of a conventional systemic agent is not required;

6. Trial and failure of at least two (2) of the following agents: Humira®, Simponi® or Stelara® ,unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed following (a or b):
   a. For Xeljanz® 20 mg per day;
   b. For Xeljanz® XR 22 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

E. Polyarticular Course Juvenile Idiopathic Arthritis (must meet all):
1. Diagnosis of pcJIA;
2. Request is for Xeljanz® tablets or Xeljanz® oral solution;
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 2 years;
5. Trial and failure of a ≥ 3 months of at least one (1) conventional systemic therapy (methotrexate [MTX] or leflunomide [Arava®]) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   *Exception: If one biologic DMARD that is FDA-approved for rheumatoid arthritis has been previously tried, then trial of a conventional systemic agent is not required;
6. Trial and failure of Humira® unless contraindicated or clinically significant adverse effects are experienced;
   *Exception: If a total of two TNF inhibitors (Humira, Simponi Aria, Enbrel®) has previously been tried and failed, trial of a third TNF inhibitor is not required.
7. Dose does not exceed following (a or b):
   a. For Xeljanz® tablets:10 mg per day;
   b. For Xeljanz® oral solution: 10 mL per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed following (a, b or c):
   a. For RA, PsA, AS: Xeljanz® tablets-10 mg per day, Xeljanz® XR-11 mg per day;
   b. For UC: Xeljanz® tablets-20 mg per day, Xeljanz® XR-22 mg per day;
   c. For pcJIA: Xeljanz® tablets 10 mg per day, Xeljanz® oral solution 10 mL per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AS: Ankylosing Spondylitis
NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

PsA: Psoriatic Arthritis
RA: Rheumatoid Arthritis
TNF: Tumor necrosis factor
DMARDs: Disease-Modifying Antirheumatic Drugs
pcJIA: Polyarticular Course Juvenile Idiopathic Arthritis
MTX: Methotrexate
UC: Ulcerative Colitis
ANC: absolute neutrophil count

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan®, Imuran®)	**RA:** 1 mg/kg/day orally once daily or divided twice daily	2.5 mg/kg/day
d-penicillamine (Cuprimine®)	**RA:** Initial dose: 125 or 250 mg orally once daily Maintenance dose: 500 – 750 mg/day orally once daily	1,500 mgc/day
cyclosporine (Sandimmune®, Neoral®)	**RA:** 2.5 – 4 mg/kg/day orally divided twice daily	RA: 4 mg/kg/day
hydroxychloroquine (Plaquenil®)	**RA:** Initial dose: 400 – 600 mg/day orally once daily Maintenance dose: 200 – 400 mg/day orally once daily	600 mg/day
leflunomide (Arava®)	**PJIA*** Weight < 20 kg: 10 mg every other day Weight 20 - 40 kg: 15 mg/day Weight > 40 kg: 20 mg/day **RA:** 100 mg orally once daily for 3 days, then 20 mg orally once daily	PJIA, RA: 20 mg/day
methotrexate	**PJIA:** 10 – 20 mg/m^2/week orally, subcutaneously, or intramuscularly **RA:** 7.5 mg/week orally, subcutaneously, or intramuscularly **PsA*:** 7.5 mg orally or subcutaneously once weekly initially, then slowly titrate to the common target dose of 15 mg orally or subcutaneously once weekly.	**PJIA:** 30 mg/m^2/week **RA**: 20 mg/week **PsA**: 25 mg/week
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS:** Varies	Varies
Ridaura®	**RA:** 6 mg orally once daily or 3 mg orally twice daily	9 mg/day (3 mg Three

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
		times daily)
sulfasalazine (Azulfidine®)	**PJIA*:** 30-50 mg/kg/day orally divided twice daily **RA:** 500 mg to 1,000 mg orally per day for the first week. Increase the daily dose up to a maintenance dose of 2 grams/day.	PJIA: 2 g/day RA: 3 g/day UC: 4 g/day
	UC: <u>Initial dose:</u> Adults: 3 – 4 g/day orally in divided doses (at least every 8 hours) Pediatrics: 40 – 60 mg/kg/day orally in 3 –6 divided doses <u>Maintenance dose:</u> Adults: 2 g orally once daily Pediatrics: 30 mg/kg/day orally in 4 divided doses	
Biologic DMARDs		
Humira®	**RA:** 40 mg subcutaneously every other week. Some patients with RA not receiving concomitant methotrexate may benefit from increasing the frequency to 40 mg every Week or 80 mg every other week **PJIA:** Children and Adolescents 4 to 17 years weighing 30 kg or more: 40 mg subcutaneously every other week Children 2 to 12 years and weighing 15 to 29 kg: 20 mg subcutaneously every other week children 2 to 12 years and weighing 10 to 14 kg: 10 mg subcutaneously every other week **AS, PsA:** 40 mg subcutaneously every other week **<u>UC:</u>** <u>Initial dose:</u> Adults:160 mg subcutaneously on Day 1 (given in one day or split over two consecutive days), then 80 mg subcutaneously on Day 15 Pediatrics: Weight 20 kg (44 lbs) to < 40 kg (88 lbs): 80 mg subcutaneously on Day 1, then 40 mg subcutaneously on Day 8, then 40 mg subcutaneously on day Day 15 Weight ≥ 40 kg (88 lbs): 160 mg subcutaneously Day 1, then 80 mg on day 8 and day 15 <u>Maintenance dose:</u> Adults: 40 mg subcutaneously every other week starting on Day 29 Pediatrics: Weight 20 kg (44 lbs) to < 40 kg (88 lbs): 40 mg every other week or 20 mg every week starting on day 29	RA, PJIA, AS, PsA: 40 mg every other week **UC:** Varies (refer full prescribing information)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Weight ≥ 40 kg (88 lbs): 80 mg every other week or 40 mg every week starting on day 29	
Cosentyx®	**PsA:** Adults: 300 mg subcutaneously at weeks 0, 1, 2, 3, and 4. Then give 300 mg subcutaneously every 4 weeks Children and Adolescents 2 to 17 years weighing 50 kg or more: 150 mg subcutaneously at weeks 0, 1, 2, 3, and 4. Then give 150 mg subcutaneously every 4 weeks. Children and Adolescents 2 to 17 years weighing 15 to 49 kg: 75 mg subcutaneously at weeks 0, 1, 2, 3, and 4. Then give 75 mg subcutaneously every 4 weeks **AS:** With loading dose: 150 mg subcutaneously at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter Without loading dose: 150 mg subcutaneously every 4 weeks.	PsA, AS: 300 mg subcutaneously/ dose
Actemra®	**RA:** Intravenous dosage: 4 mg/kg intravenously infusion given over 1 hour every 4 weeks. Subcutaneous dosage: Adults weighing less than 100 kg: 162 mg subcutaneously every other week, increase to 162 mg subcutaneously once weekly based on clinical response Adults weighing 100 kg or more: 162 mg subcutaneously once weekly **PJIA:** Intravenous dosage: Children and Adolescents 2 to 17 years weighing 30 kg or more: 8 mg/kg/dose intravenously every 4 weeks; administer over 1 hour Children and Adolescents 2 to 17 weighing less than 30 kg: 10 mg/kg/dose intravenously every 4 weeks; administer over 1 hour. Subcutaneous dosage: Children and Adolescents 2 to 17 years weighing 30 kg or more: 162 mg/dose subcutaneously every 2 weeks. Children and Adolescents 2 to 17 years weighing less than 30	RA: 800 mg per intravenous infusion. 162 mg subcutaneously once weekly PJIA: 10 mg/kg/dose intravenously. 162 mg/dose subcutaneously

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	kg: 162 mg/dose subcutaneously every 3 weeks.	
Cimzia®	**RA, PsA:** 400 mg subcutaneously, at weeks 0, 2, and 4 then 200 mg subcutaneously every other week **AS:** 400 mg subcutaneously at weeks 0, 2, and 4, then 200 mg subcutaneously every 2 weeks or 400 mg subcutaneously every 4 weeks	400 mg/dose subcutaneously.
Enbrel®	**RA, PsA:** 25 mg subcutaneously twice weekly or 50 mg subcutaneously once weekly **AS:** 50 mg subcutaneously once weekly **PJIA:** Weight < 63 kg: 0.8 mg/kg subcutaneously once weekly Weight ≥ 63 kg: 50 mg subcutaneously once weekly	50 mg/week
Entyvio®	**UC:** Initial dose: 300 mg intravenously at weeks 0, 2, and 6 Maintenance dose: 300 mg intravenously every 8 weeks	300 mg every 8 weeks
Infliximab (Remicade®), Renflexis®, Inflectra®, Avsola®	**UC:** Initial dose: 5 mg/kg intravenously at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg intravenously every 8 weeks. **PsA:** Initial dose: 5 mg/kg intravenously at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg intravenously every 8 weeks **RA:** In conjunction with MTX Initial dose: 3 mg/kg intravenously at weeks 0, 2 and 6 Maintenance dose: 3 mg/kg intravenously every 8 weeks Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks **AS:** Initial dose: 5 mg/kg intravenously at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg intravenously every 6 weeks	UC: 5 mg/kg every 8 weeks PsA: 5 mg/kg every 8 weeks RA: 10 mg/kg every 4 weeks AS: 5 mg/kg every 6 weeks
Kevzara®	**RA:** 200 mg subcutaneously once every two weeks	200 mg/2 Weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Kineret®	**RA:** 100 mg subcutaneously once daily	100 mg/day
Olumiant®	**RA:** 2 mg orally once daily	2 mg/day
Orencia®	**PJIA:** Intravenous dosage: in pediatric patients ≥ 6 years old weight-based dose at weeks 0, 2, and 4, followed by every 4 weeks Weight < 75 kg: 10 mg/kg per dose Weight 75 to 100 kg: 750 mg per dose Weight >100 kg: 1,000 mg per dose Subcutaneous dosage: In pediatric patients ≥ 2 years old weight-based dose once weekly Weight 10 to < 25 kg: 50 mg per dose Weight 25 to < 50 kg: 87.5 mg per dose Weight ≥ 50 kg: 125 mg per dose **RA, PsA:** Intravenous dosage: weight-based dose at weeks 0, 2, and 4, followed by every 4 weeks Weight < 60 kg: 500 mg per dose Weight 60 to 100 kg: 750 mg per dose Weight > 100 kg: 1,000 mg per dose Subcutaneous dosage: 125 mg once weekly RA and PsA: Patients switching from intravenous use to subcutaneous use, administer first subcutaneous dose instead of next scheduled intravenous dose. (For RA: Prior to the first subcutaneous dose, may administer an optional loading dose as a single intravenous infusion as per body weight categories above.) For PsA: Intravenous loading dose is not recommended	PJIA: Intravenous: 1,000 mg every 4 weeks Subcutaneous: 125 mg/week RA, PsA: Intravenous: 1,000 mg every 4 weeks Subcutaneous: 125 mg/week
Otezla®	<u>Initial dose:</u> Day 1: 10 mg orally in morning Day 2: 10 mg orally in morning and 10 mg orally in evening Day 3: 10 mg orally in morning and 20 mg orally in evening Day 4: 20 mg orally in morning and 20 mg orally in evening Day 5: 20 mg orally in morning and 30 mg orally in evening <u>Maintenance dose:</u> Day 6 and thereafter: 30 mg orally twice daily	60 mg/day
Rinvoq®	**RA, PsA:** 15 mg orally once daily Can be used as monotherapy or in combination with methotrexate or other non-biologic DMARDs.	15 mg/day
Simponi®	**AS, PsA, RA:** 50 mg subcutaneous once monthly	AS, PxA, RA: 50 mg/month

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	UC: Initial dose: 200 mg subcutaneously at week 0, then 100 mg subcutaneously at week 2 Maintenance dose: 100 mg subcutaneously every 4 weeks	UC: 100 mg every 4 weeks
Skyrizi®	**PsA:** 150 mg administered by subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter	150 mg every 12 weeks
Simponi Aria®	**AS, PsA, RA:** Initial dose: 2 mg/kg intravenously at weeks 0 and 4 Maintenance dose: 2 mg/kg intravenously every 8 weeks **PJIA:** Initial dose: 80 mg/m^2 at weeks 0 and 4 Maintenance dose: 80 mg/m^2 intravenously every 8 weeks	AS, PxA, RA: 2 mg/kg every 8 weeks PJIA: 80 mg/m^2 every 8 weeks
Stelara®	**PsA:** 45 mg subcutaneously at weeks 0 and 4, followed by 45 mg every 12 weeks **UC:** Weight based dosing intravenously at initial dose, followed by 90 mg subcutaneously every 8 weeks Weight ≤ 55 kg: 260 mg Weight 55 kg to 85 kg: 390 mg Weight > 85 kg: 520 mg	PsA: 45 mg every 12 weeks UC: 90 mg every 8 weeks
Taltz®	**PsA, AS:** Initial dose: 160 mg (two 80 mg injections) subcutaneously Maintenance dose: 80 mg subcutaneously every 4 weeks	PsA, AS: 80 mg every 4 weeks
Tremfya®	**PsA:** Initial dose: 100 mg subcutaneously at weeks 0 and 4 Maintenance dose: 100 mg subcutaneously every 8 weeks Can be used alone or in combination with conventional DMARD e.g. methotrexate	100 mg every 8 weeks

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - Serious infections
  - Mortality
  - Malignancy
  - Major Adverse Cardiovascular Events (MACE)
  - Thrombosis.

APPENDIX D: General Information

- Ankylosing Spondylitis:
  - Several AS treatment guidelines call for a trial of 2 or 3 NSAIDs prior to use of an anti- TNF agent. A two-year trial showed that continuous NSAID use reduced radiographic progression of AS versus on demand use of NSAID.
- Ulcerative Colitis:
  - For UC maintenance therapy, failure is defined as having two or more exacerbations requiring steroid therapy.
- Polyarticular Juvenile Idiopathic Arthritis:
  - Failure of MTX in PCJIA is defined as disease activity remaining moderate to high despite treatment with MTX.
  - In PCJIA, response to treatment is reflected by improvement of disease activity level and poor prognostic features including reduction in the number of active joints, ESR or CRP, Physician global assessment, patient/parent global assessment, arthritis of the hip or cervical spine, positive RF or ACPA, radiographic damage.
- Per prescribing information, tofacitinib should not be used in combination with biologic DMARDs [such as anakinra] or potent immunosuppressants such as azathioprine and cyclosporine. As stated in the black box warning, patients treated with tofacitinib are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as MTX or corticosteroids.
- Use of tofacitinib in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
- Do not initiate tofacitinib if absolute lymphocyte count <500 cells/mm^3, an absolute neutrophil count (ANC) <1000 cells/mm^3 or hemoglobin <9 g/dL.
- Use of tofacitinib in patients with severe hepatic impairment is not recommended in any patient population.
- Avoid use of tofacitinib in patients with an active, serious infection, including localized infections.
- PsA: According to the 2019 American College of Rheumatology TNF inhibitors is recommended over other biologics for use in treatment-naïve patients with psoriatic arthritis, and in those who were previously treated with an oral therapy.
- MTX is a pregnancy category X and is absolutely contraindicated in pregnancy and is not recommended for female patients attempting to conceive.

References

1. Xeljanz®/Xeljanz® XR/Xeljanz® oral Solution Prescribing Information. New York, NY: Pfizer Labs. January 2022. Available at: https://www.xeljanz.com/. Accessed February 16, 2022.
2. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid Arthritis Classification Criteria. Arthritis and Rheumatism September 2010;62(9):2569-2581. Available at: https://pubmed.ncbi.nlm.nih.gov/20872595/. Accessed February 16, 2022.
3. Boulos P, Dougados M, MacLeod SM, et al. Pharmacological Treatment of Ankylosing Spondylitis. Drugs. 2005; 65: 2111-2127. Available at: https://pubmed.ncbi.nlm.nih.gov/16225367/. Accessed February 16, 2022.
4. Braun J, Davis J, Dougados M, et al. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with ankylosing spondylitis. Ann Rheum Dis. 2006; 65:316-320. Available at: https://pubmed.ncbi.nlm.nih.gov/16096329/. Accessed February 16, 2022.
5. Braun J, van den Berg R, Baraliako X, et al. 2010 Update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2011; 70:896-904. Available at: https://pubmed.ncbi.nlm.nih.gov/21540199/. Accessed February 16, 2022.
6. Ward M, Deodhar A, Akl E, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Available at: http://www.rheumatology.org. Accessed February 16, 2022.
7. Menter A, Gottlieb A, Feldman SR, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008; 58:826-850. Available at: https://www.jaad.org/article/S0190-9622(08)00273-9/fulltext. Accessed February 16, 2022.
8. Menter A, Gottlieb A, Feldman, SR, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol May 2008; 58(5): 826-50. Available at: https://pubmed.ncbi.nlm.nih.gov/18423260/. Accessed February 16, 2022.
9. Menter A, Korman NF, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol. 10.1016/j.jaad.2009.03.027. Available at: https://pubmed.ncbi.nlm.nih.gov/19493586/. Accessed February 16, 2022.
10. Menter A, Korman, NJ, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol. 2009; 60:643-659. Available at: https://pubmed.ncbi.nlm.nih.gov/19217694/. Accessed February 16, 2022.
11. Zochling J, van der Heijde D, Burgos-Vargas, R, et al. ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis. 2006; 65:442-452. Available at: https://pubmed.ncbi.nlm.nih.gov/16126791/. Accessed February 16, 2022.
12. 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. Available at: https://pubmed.ncbi.nlm.nih.gov/26644232/. Accessed February 16, 2022.
13. 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. Available at: https://pubmed.ncbi.nlm.nih.gov/30499246/. Accessed February 16, 2022.
14. Tofacitinib. Lexi-Drug. Lexicomp. Wolters Kluwer. Hudson, OH. Available at: http://online.lexi.com. Accessed February 16, 2022.
15. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 16, 2022.
16. Tofacitinib. Micromedex Solutions. Truven Health Analtics Inc. Greenwood Village, CO. Available at:

http://www.micromedexsolutions.com. Accessed February 16, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
RxA.592.Biologic_DMARDs was last reviewed and updated on 01/05/2022 and archived on 04/18/2022. For details, please refer to RxA.592.Biologic_DMARDs.	01/05/2022	04/18/2022
Drug specific policy for Xeljanz_Xeljanz XR was created based on RxA.592.Biologic_DMARDs 1. Dosing Information, Dosing Regimen, Xelianz®: Updated to include renal and hepatic impairment dosing information for indication UC, PsA, RA, AS. 2. Dosing Information, Dosing Regimen, Xelianz® XR: Updated to include renal and hepatic impairment dosing information for indication UC, PsA, RA, AS. 3. Dosing Information, Dosing Regimen, Xelianz® oral solution: Updated to include renal and hepatic impairment dosing information for indication pcJIA. 4. Initial Approval Criteria, I.A.6 and I.B.5: Updated to include new trial and failure criteria Trial and failure of a ≥ 3 months of at least one (1) TNF inhibitor (Cimzia®, Humira®, Simponi®/ Simponi Aria, Enbrel®) , unless contraindicated or clinically significant affects are experienced. 5. Initial Approval Criteria I.C.6: Updated to include new trial and failure criteria Trial and failure of at least two (2) of the following agents: Humira®, Simponi®/ Simponi Aria®, Cimzia®, unless contraindicated or clinically significant adverse effects are experienced; *Exception: If a total of two TNF inhibitors (Humira, Cimzia®, Simponi®/ Simponi Aria, Enbrel®) has previously been tried and failed, trial of a third TNF inhibitor is not	2/16/2022	04/18/2022

required. 6. Initial Approval Criteria I.D.6: Updated to include new trial and failure criteria Trial and failure of at least two (2) of the following agents: Humira®, Simponi®/ Simponi Aria®, Cimzia®, unless contraindicated or clinically significant adverse effects are experienced. 7. Initial Approval Criteria, I.E.5: Updated to remove prior trial and failure criteria "Failure of a trial of ≥ 3 months of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced". 8. Initial Approval Criteria, I.E.5: Updated to include new trial and failure criteria Trial and failure of a ≥ 3 months of at least one (1) conventional systemic therapy (methotrexate [MTX] or leflunomide [Arava®]) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced; *Exception: If one biologic DMARD that is FDA-approved for rheumatoid arthritis has been previously tried, then trial of a conventional systemic agent is not required. 9. Initial Approval Criteria, I.E.6: Updated to include new trial and failure criteria "Trial and failure of Humira® unless contraindicated or clinically significant adverse effects are experienced; *Exception: If a total of two TNF inhibitors (Humira, Simponi Aria, Enbrel®) has previously been tried and failed, trial of a third TNF inhibitor is not required". 10. Appendix B, Drug Name: Updated to include brand-name therapeutic		

alternative of other biological DMARDs. 11. Appendix D, General Information: Updated to remove information regarding: (a, b, c and d) a. Rheumatoid Arthritis b. Ulcerative Colitis; c. Definition of failure of MTX or DMARDs; d. Examples of positive response to therapy 12. Reference were reviewed and updated.		