AETNA BETTER HEALTH®
Coverage Policy/Guideline

Name:	Xeljanz-Xeljanz XR	Page:	1 of 9
Effective Date:	9/28/2023	Last Review Date:	7/20/2023

Applies to:	☐Illinois	☐Florida	☒Florida Kids
	☒New Jersey	☒Maryland	☐Michigan
	☒Pennsylvania Kids	☐Virginia	☐Kentucky PRMD

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for Xeljanz/Xeljanz XR under the patient's prescription drug benefit.

Description:

A. FDA-Approved Indications
   1. Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers.
   2. Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers.
   3. Xeljanz/Xeljanz XR is indicated for the treatment of adult patients with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers.
   4. Xeljanz/Xeljanz XR is indicated 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.
   5. Xeljanz/Xeljanz Oral Solution is indicated 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.

B. Compendial Uses
   1. Non-radiographic axial spondyloarthritis
   2. Oligoarticular juvenile idiopathic arthritis
   3. Immune checkpoint inhibitor related toxicity

All other indications are considered experimental/investigational and not medically necessary.

Applicable Drug List:

Non-Preferred:
Xeljanz
Xeljanz XR

Policy/Guideline:

Documentation for all indications:
The patient is unable to take ONE preferred anti-TNF (Enbrel or preferred adalimumab product) AND Kevzara, where indicated, for the given diagnosis due to a trial and inadequate treatment response or intolerance, or a contraindication. Documentation is required for approval.

Documentation:

A. **Rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), and articular juvenile idiopathic arthritis (JIA)**
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. **Ulcerative colitis (UC)**
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

C. **Immune checkpoint inhibitor-related toxicity:** Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy or intolerance to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

Prescriber Specialty:
This medication must be prescribed by or in consultation with one of the following:

A. Rheumatoid arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, and articular juvenile idiopathic arthritis: rheumatologist
B. Psoriatic arthritis: rheumatologist or dermatologist
C. Ulcerative colitis: gastroenterologist
D. Immune checkpoint inhibitor related toxicity: hematologist or oncologist

Criteria for Initial Approval:

A. Rheumatoid arthritis (RA)
   1. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active rheumatoid arthritis (RA) when the member has

experienced an inadequate response or intolerance to at least one tumor necrosis factor (TNF) inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq, Olumiant) indicated for moderately to severely active RA.

B. Psoriatic arthritis (PsA)

1. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when both of the following criteria are met:
   i. The requested drug will be used in combination with a conventional synthetic drug (e.g., methotrexate, leflunomide, sulfasalazine).
   ii. Member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when both of the following criteria are met:
   i. The requested drug will be used in combination with a conventional synthetic drug (e.g., methotrexate, leflunomide, sulfasalazine).
   ii. Member has previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.

C. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

1. Authorization of 12 months may be granted for adult members for treatment of active ankylosing spondylitis or active non-radiographic axial spondyloarthritis when the member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq) indicated for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis.

D. Ulcerative colitis (UC)

1. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active UC when the member has had an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for adult members who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug (e.g., Rinvoq) indicated for moderately to severely active ulcerative colitis.

E. Articular juvenile idiopathic arthritis (JIA)

1. Authorization of 12 months may be granted for members 2 years of age or older for treatment of active articular juvenile idiopathic arthritis when the member has experienced an inadequate response or intolerance to at least one TNF inhibitor.

2. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic (other than a TNF inhibitor) or targeted synthetic drug indicated for active articular juvenile idiopathic arthritis.

F. Immune checkpoint inhibitor-related toxicity

Authorization of 1 month may be granted for treatment of immune checkpoint inhibitor-related colitis when the member has experienced an inadequate response, intolerance, or contraindication to infliximab or vedolizumab.

Continuation of Therapy:

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Psoriatic arthritis (PsA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease

6. Skin and/or nail involvement

C. Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)

D. Ulcerative colitis (UC)

1. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Stool frequency
   ii. Rectal bleeding
   iii. Urgency of defecation
   iv. C-reactive protein (CRP)
   v. Fecal calprotectin (FC)
   vi. Endoscopic appearance of the mucosa
   vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

E. Articular juvenile idiopathic arthritis (JIA)

Authorization of 12 months may be granted for all members 2 years of age and older (including new members) who are using the requested medication for active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

F. Immune checkpoint inhibitor-related toxicity

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

Other Criteria:
Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

*If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested drug to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested drug.

Member cannot use the requested medication concomitantly with any other biologic drugs, targeted synthetic drugs, or potent immunosuppressants such as azathioprine or cyclosporine.

Approval Duration and Quantity Restrictions:
Approval:
Initial Approval: 1 month (for Immune checkpoint inhibitor-related toxicity), 12 months for all other indications
Renewal Approval: 1 month (for Immune checkpoint inhibitor-related toxicity), 12 months for all other indications

Quantity Level Limit:
Xeljanz 5 mg tablet: 60 tablets per 30 days
Xeljanz 10 mg tablet: 60 tablets per 30 days
Xeljanz XR 11 mg tablet: 30 tablets per 30 days
Xeljanz XR 22 mg tablet: 30 tablets per 30 days
Xeljanz oral solution 1 mg/mL: 240 mL (1 bottle) per 24 days

Xeljanz FDA-Recommended Dosing:

RA/PsA/pcJIA/AS:

- 5 mg twice daily (for pcJIA, if body weight ≥ 40 kg)
- Dose adjustment: reduce to 5 mg once daily for patients:
  - Receiving strong CYP3A4 inhibitors
  - Receiving a moderate CYP3A4 inhibitor with a strong CYP2C19 inhibitor (coadministration with strong CYP3A4 inducer is not recommended)
  - With moderate or severe renal impairment
  - With moderate hepatic impairment (not recommended for patients with severe hepatic impairment)

Ulcerative colitis:

Induction

10 mg twice daily for at least 8 weeks; evaluate patients and transition to maintenance therapy depending on therapeutic response. If needed, continue 10 mg twice daily for a maximum of 16 weeks. Discontinue 10 mg twice daily after 16 weeks if adequate therapeutic response is not achieved.

Maintenance

5 mg twice daily. For patients with loss of response during maintenance treatment, a dosage of 10 mg twice daily may be considered and limited to the shortest duration, with careful consideration of the benefits and risks for the individual patient. Use the lowest effective dose needed to maintain response.

Dose Adjustments

If taking 10 mg twice daily reduce to 5 mg twice daily and if taking 5 mg twice daily reduce to 5 mg once daily for patients:

- Receiving strong CYP3A4 inhibitors
- Receiving a moderate CYP3A4 inhibitor with a strong CYP2C19 inhibitor (coadministration with strong CYP3A4 inducer is not recommended)
- With moderate or severe renal impairment
- With moderate hepatic impairment (not recommended for patients with severe hepatic impairment)

Xeljanz XR 11 mg tablet FDA-Recommended Dosing for RA/PsA/UC/AS:

- 11 mg once daily
- Dose adjustment: reduce to 5 mg once daily for patients:
  - Receiving strong CYP3A4 inhibitors
  - Receiving a moderate CYP3A4 inhibitor with a strong CYP2C19 inhibitor (coadministration with strong CYP3A4 inducer is not recommended)

- With moderate or severe renal impairment
- With moderate hepatic impairment
  (not recommended for patients with severe hepatic impairment)

Xeljanz XR 22 mg tablet FDA-Recommended Dosing for Ulcerative Colitis:

Induction:

22 mg once daily for at least 8 weeks; evaluate patients and transition to maintenance therapy depending on therapeutic response. If needed continue 22 mg once daily for a maximum of 16 weeks. Discontinue 22 mg once daily after 16 weeks if adequate therapeutic response is not achieved.

Maintenance:

11 mg once daily. For patients with loss of response during maintenance treatment, a dosage of 22 mg once daily may be considered and limited to the shortest duration, with careful consideration of the benefits and risks for the individual patient. Use the lowest effective dose needed to maintain response.

Dose Adjustments

If taking 22 mg once daily reduce to 11 mg once daily and if taking 11 mg once daily reduce to 5 mg once daily for patients:

- Receiving strong CYP3A4 inhibitors
- Receiving a moderate CYP3A4 inhibitor with a strong CYP2C19 inhibitor
  (coadministration with strong CYP3A4 inducer is not recommended)
- With moderate or severe renal impairment
- With moderate hepatic impairment
  (not recommended for patients with severe hepatic impairment)

Xeljanz oral solution 1 mg/mL FDA-Recommended Dosing for pcJIA:

- 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 (5 mL oral solution) twice daily
- Dose adjustment: reduce to once daily dosing for patients:
  - Receiving strong CYP3A4 inhibitors
  - Receiving a moderate CYP3A4 inhibitor with a strong CYP2C19 inhibitor
    (coadministration with strong CYP3A4 inducer is not recommended)
  - With moderate or severe renal impairment
  - With moderate hepatic impairment (not recommended for patients with severe hepatic impairment)

References:

1. Xeljanz/Xeljanz XR [package insert]. New York, NY: Pfizer, Inc.; January 2022.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
3. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis*. 2020;79:685-699.
4. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
5. 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.* 2016;75(3):499-510.
6. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol.* 2011;106(Suppl 1):S2-S25.
7. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheum*. 2018;71:5-32.
8. Rubin DT, Ananthakrishnan AN, et al. 2019 ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroentrol*. 2019;114:384-413.
9. Testing for TB Infection. Centers for Disease Control and Prevention. Retrieved on June 15, 2022 from: https://www.cdc.gov/tb/topic/testing/tbtesttypes.htm.
10. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. *Gastroenterology* 2020; 158:1450.
11. Ringold S, Angeles-Han S, 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 (Hoboken).* 2019; 71(6):717-734.
12. Aletaha D, Neogi T, Silman, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-81.
13. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthrit Care Res*. 2021.
14. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 17, 2022.
15. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol.* 2019;71(10):1599-1613. doi:10.1002/art.41042.
16. Gossec L, Baraliakos X, Kerschbaumer A. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Ann Rheum Dis*. 2020;79(6):700-712.
17. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
18. Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for oligoarthritis, temporomandibular joint arthritis, and systemic juvenile idiopathic arthritis. *Arthritis Rheumatol*. 2022;74(4):553-569.
19. Coates LC, Soriano ER, Corp N, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. *Nat Rev Rheumatol.* 2022;18(8):465-479.