MEDICAL MUTUAL®

Drug Policy

Policy:	Rinvoq (Upadacitinib)	Annual Review Date: 06/15/2023 Last Revised Date: 06/15/2023

OVERVIEW

Rinvoq is a Janus kinase (JAK) inhibitor indicated for treatment of adults with moderately to severely active rheumatoid arthritis, ulcerative colitis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, atopic dermatitis, crohn's disease and the treatment of psoriatic arthritis. Rinvoq is also indicated for treatment of atopic dermatitis in patients 12 years of age or older. In RA, Rinvoq inhibits JAK, an intracellular enzyme that transmits signals on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STAT) which then modulate intracellular activity such as gene expression. Inhibition of JAK block multiple cytokines resulting in modulation of the immune response involved in RA.

The efficacy of Rinvoq over placebo was established in five pivotal studies that included a variety of clinical scenarios, including Rinvoq as monotherapy or in combination with MTX or other conventional synthetic DMARDs and in patients who had previously failed a biologic.

Rinvoq has Boxed Warnings regarding increased risk of developing serious infections which may lead to hospitalization or death. Patients who develop a serious infection should interrupt treatment with Rinvoq until infection is controlled. Patients should be tested for tuberculosis (TB) prior to starting therapy and monitored during treatment with Rinvoq. There is also a Boxed Warning for lymphoma and other lymphoproliferative disorders which have been observed in patients taking Rinvoq. Viral reactivation, including cases of herpes virus reactivation, have been reported. Rinvoq also has a Boxed Warning regarding thrombosis, including deep vein thrombosis and pulmonary embolism which occurred in patients treated with other JAK inhibitors used to treat inflammatory conditions.

POLICY STATEMENT

This policy involves the use of Rinvoq. Prior authorization is recommended for pharmacy benefit coverage of Rinvoq. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Rinvoq as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Rinvoq be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided

for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below. **Rinvoq is subject to the Inflammatory Conditions Care Value Program under pharmacy benefits**

All reviews for use of Rinvoq for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Rinvoq is recommended in those who meet the following criteria:

1. **Crohn's Disease**
   - **A)** Initial Therapy. Approve is the patient meets all the following criteria (i, ii, iii and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets one of the following conditions (a or b)
       - **a)** The patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
       - **b)** The patient has tried one conventional systemic therapy for Crohn's disease for at least 3 months (e.g., azathioprine, 6-mercaptopurine, or methotrexate [MTX]; AND
     - **iii.** Rinvoq is prescribed by or in consultation with a gastroenterologist; AND
     - **iv.** The patient has trialed 1 TNF-inhibitor indicated for Crohn's disease (adalimumab products, Cimzia) for at least 3 months and was unable to achieve an adequate response or a TNF-inhibitor is contraindicated.
   - **B)** Patient is currently receiving Rinvoq**.** Approve if the patient meets BOTH the following (i and ii):
     - **i.** Patient has been established on therapy for at least 6 months; AND
       Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
     - **ii.** The provider attests that the patient has achieved an adequate response to therapy

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months (180 days)*
B) *Extended Approval: 1 year (365 days)*

2. **Ankylosing Spondylitis**. Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets ONE of the following (a or b):
       - **a)** Patient has had a 3-month trial of at least ONE tumor necrosis factor inhibitor; OR
       - **b)** Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND
         Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for rheumatoid arthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.
     - **iii.** The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Rinvoq. Approve if the patient meets BOTH the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Rinvoq); OR
Note: Examples of objective measures include Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), Health Assessment Questionnaire for the Spondylarthropathies (HAQ-S), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

Compared with baseline (prior to initiating Rinvoq), patient experienced an improvement in at least one symptom, such as decreased pain or stiffness, or improvement in function or activities of daily living.

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months (180 days)*
B) *Extended Approval: 1 year (365 days)*

3. Non-Radiographic Axial Spondyloarthritis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets the following (i, ii and iii):

i. Patient has objective signs of inflammation, defined as at least one of the following (a or b):
a) C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory; OR
b) Sacroiliitis reported on magnetic resonance imaging (MRI); AND

ii. Patient meets ONE of the following (a or b):
a) Patient has had a 3-month trial of at least ONE tumor necrosis factor inhibitor; OR
b) Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND
Note: Cimzia (certolizumab pegol subcutaneous injection) is an example of tumor necrosis factor inhibitor used for non-radiographic axial spondyloarthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.

iii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Rinvoq. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on the requested drug for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with the requested drug is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include Ankylosing Spondylitis Disease Activity Score (ASDAS), Ankylosing Spondylitis Quality of Life Scale (ASQoL), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global Score (BAS-G), Bath Ankylosing Spondylitis Metrology Index (BASMI), Dougados Functional Index (DFI), Health Assessment Questionnaire for the Spondylarthropathies (HAQ-S), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain or stiffness, or improvement in function or activities of daily living

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months (180 days)*
B) *Extended Approval: 1 year (365 days)*

4. Atopic Dermatitis. Approve for the duration noted if the patient meets one of the following (A or B):

A) Initial Therapy. Approve if the patient meets the following criteria (i, ii, iii, iv, v and vi):

i. Patient is ≥ 12 years of age; AND

ii. Patient has moderate-to-severe atopic dermatitis with at least one of the following (a, b, c, d, or e):

a) Involvement of at least 10% of body surface area (BSA); OR

b) Eczema Area and Severity Index (EASI) score of 16 or greater; OR

c) Investigator's Global Assessment (IGA) score of 3 or more; OR

d) Scoring Atopic Dermatitis (SCORAD) score of 25 or more; OR

e) Incapacitation due to AD lesion location; AND

iii. The medication is prescribed by or in consultation with an allergist, immunologist, or dermatologist.

iv. The patient did not have an adequate response or is intolerant to a 3-month trial of one topical corticosteroid; AND

v. The patient did not have an adequate response or is intolerant to a 3-month trial of one topical calcineurin inhibitor; AND

vi. Patient did not have an adequate response or is intolerant to at least one systemic agent (e.g., cyclosporine, azathioprine, methotrexate, mycophenolate mofetil OR phototherapy)

B) Patient is Currently Receiving Rinvoq. Approve if the patient meets the following (i, ii, and iii):

i. Patient has already received at least 180 days of therapy with Rinvoq; AND
Note: A patient who has received > 180 days of therapy or who is restarting therapy with Rinvoq should be considered under Initial Therapy.

ii. Patient experienced a beneficial clinical response, defined as improvement from baseline (prior to initiating Rinvoq) in at least one of the following: estimated body surface area affected, erythema, induration/papulation/edema, excoriations, lichenification, and/or a decreased requirement for other topical or systemic therapies for atopic dermatitis; AND

iii. Compared with baseline (prior to receiving Rinvoq), patient experienced an improvement in at least one symptom, such as decreased itching.

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months (180 days)*
B) *Extended Approval: 1 year (365 days)*

4. Rheumatoid Arthritis (RA).
Criteria. *Patient must meet the following criteria*

A) Initial Therapy. The patient must meet ALL the following (i, ii and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has had a 3-month trial of at least ONE tumor necrosis factor inhibitor; OR
  - **b)** Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND

  Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for rheumatoid arthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.
- **iii.** The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Rinvoq. Approve if the patient meets BOTH of the following (i and ii):
- **1.** Patient has been established on the requested drug for at least 6 months; AND

  Note: A patient who has received < 6 months of therapy or who is restarting therapy with the requested drug is reviewed under criterion A (Initial Therapy).
- **2.** Patient meets at least one of the following (a or b):
  - **a)** Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR

    Note: Examples of standardized and validated measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).
  - **b)** Patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months (180 days)*
B) *Extended Approval: 1 year (365 days)*

5. Psoriatic Arthritis. Approve if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL the following criteria (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has had a 3-month trial of at least ONE tumor necrosis factor (TNF) inhibitor; OR

b) Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND
Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for psoriatic arthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.

iii. The medication is prescribed by or in consultation with a rheumatologist or a dermatologist.

B) Patient is Currently Receiving Rinvoq. Approve if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Rinvoq); OR
Note: Examples of standardized measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortuium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

b) Compared with baseline (prior to initiating Rinvoq), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function, or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months (180 days)*
B) *Extended Approval: 1 year (365 days)*

6. Ulcerative Colitis. Approve if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following criteria (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient meets ONE of the following (a or b):

a) Patient has had a 3-month trial of at least ONE tumor necrosis factor (TNF) inhibitor; OR

b) Patient has tried at least one tumor necrosis factor inhibitor but was unable to tolerate a 3-month trial; AND
Note: Refer to Appendix for examples of tumor necrosis factor inhibitors used for psoriatic arthritis. Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.

iii. The medication is prescribed by or in consultation with a rheumatologist or a dermatologist.

B) Patient is Currently Receiving Rinvoq. Approve if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

c) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Rinvoq); OR
Note: Examples of standardized measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortuium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

d) Compared with baseline (prior to initiating Rinvoq), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function, or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

Initial Approval/ Extended Approval.
A) *Initial Approval: 6 months (180 days)*
B) *Extended Approval: 1 year (365 days)*

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Rinvoq has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Treatment of Alopecia.** Alopecia is considered cosmetic. Cosmetic uses are excluded from coverage in a typical medical or pharmacy plan benefit.

2. **COVID-19 (Coronavirus Disease 2019).** Forward all requests to the Medical Director. Note: This includes requests for cytokine release syndrome associated with COVID.

3. **Concurrent use with Xolair® (omalizumab subcutaneous injection).** Rinvoq is not recommended in combination with biologic immunomodulators such as Xolair.[1]

4. **Use of Rinvoq in combination with another biologic DMARD**. See Appendix for examples.

5. **Use of Rinvoq in combination with another JAK inhibitor**. See Appendix for examples.

6. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Rinvoq [prescribing information]. North Chicago, IL: AbbVie; April 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. Upadacitinib. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 27 August 2019. Accessed on 12 September 2019.

Appendix

Biologic or Targeted Synthetic DMARD	Mechanism of Action	Indications
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF	AS, ASpA ,CD, PPs, PsA, RA
Enbrel® (etanercept for SC injection)	Inhibition of TNF	AS, PPs, PsA, RA
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF	AS, PPs, PsA, RA
Humira® (adalimumab for SC injection)	Inhibition of TNF	AS, CD, HS, PPs, RA, UC, UV
Amjevita™ (adalimumab-atto for SC injection)	Inhibition of TNF	AS, CD, PPs, RA, UC
Cyltezo® (adalimumab-adbm for SC injection)	Inhibition of TNF	AS, CD, PPs, RA, UC
Simponi® (golimumab for SC injection)	Inhibition of TNF	AS, PsA, RA, UC
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF	AS, PsA, RA, UC
Remicade® (infliximab for IV infusion)	Inhibition of TNF	AS, CD, PPs, PsA, RA, UC
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF	AS, CD, PPs, PsA, RA, UC
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF	AS, CD, PPs, PsA, RA, UC
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6	CRS, GCA, RA
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6	CRS, GCA, RA
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator	PsA, RA
Orencia® (abatacept for SC injection)	T-cell costimulation modulator	PsA, RA
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody	Various
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1	NOMID, RA
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23	CD, PPs, PsA, UC
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23	CD, PPs, PsA, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PPs

Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A	AS, PPs, PsA
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A	AS, PPs, PsA
Ilumya™ (tildrakizumab-asmn for SC injection)	Inhibition of IL-23	PPs
Tremfya® (guselkumab for SC injection)	Inhibition of IL-23	PPs
Otezla® (apremilast tablets)	Inhibition of PDE4	BD, PPs, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib ER tabs)	Inhibition of the JAK pathways	PsA, RA, UC

Agents and associated indications are for reference only.

"The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding."

AS = Ankylosing Spondylitis, ASpA = Axial Spondyloarthritis, BD = Behcet Disease, CD = Crohn's Disease, CRS = Cytokine Release Syndrome, GCA = Giant Cell Arteritis, GVHD = Graft-Versus-Host Disease, HS = Hidradenitis Suppurativa, NOMID = Neonatal-onset Multisystem Inflammatory Disease, PPs = Plaque Psoriasis, PsA = Psoriatic Arthritis, RA = Rheumatoid Arthritis, SpA = Spondyloarthritis, UC = Ulcerative Colitis, UV = Uveitis