Clinical Policy: Upadacitinib (Rinvoq)

Reference Number: CP.PHAR.443
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Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Upadacitinib (Rinvoq®) is a Janus kinase (JAK) inhibitor.

FDA Approved Indication(s)

Rinvoq is indicated for 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.
- Adults with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
- Adults and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable.
- Adult patients with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers.
- Adults with active ankylosing spondylitis who have had an inadequate response or intoleranace to one or more TNF blockers.
- Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation who have had an inadequate response or intolerance to TNF blocker therapy.
- Adults with moderately to severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers.

Limitation(s) of use: Use of Rinvoq in combination with other JAK inhibitors, biologic DMARDs, or with 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 Rinvoq is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (*see Appendix E*);
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 methotrexate (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 at least ONE conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless clinically significant adverse effect are experienced or all are contraindicated;
5. Failure of ALL* of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c, *see Appendix D*):
   a. One adalimumab product (e.g. *Hadlima™, Yusimry™, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), unless the member has had a history of failure of two TNF blockers;
   b. Actemra®;
   c. If member has not responded or is intolerant to one or more TNF blockers, Xeljanz®/Xeljanz XR®, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

   **Prior authorization may be required for adalimumab products, Actemra, and Xeljanz/Xeljanz XR*
6. Documentation of one of the following baseline assessment scores (a or b):
   a. Clinical disease activity index (CDAI) score (*see Appendix F*);
   b. Routine assessment of patient index data 3 (RAPID3) score (*see Appendix G*);
7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. Dose does not exceed both of the following (a and b):
   a. 15 mg per day;
   b. 1 tablet 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. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, c, and d, *see Appendix D*):
   a. One adalimumab product (e.g. *Hadlima™, Yusimry™, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), unless the member has had a history of failure of two TNF blockers;
   b. Otezla®;
   c. Taltz®;
   d. If member has not responded or is intolerant to one or more TNF blockers, Xeljanz/Xeljanz XR, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

   **Prior authorization may be required for adalimumab products, Otezla, Taltz, and Xeljanz/Xeljanz XR*

5. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
6. Dose does not exceed both of the following (a and b):
   a. 15 mg per day;
   b. 1 tablet per day.

Approval duration: 6 months

C. Atopic Dermatitis (must meet all)**:**

1. Diagnosis of atopic dermatitis affecting one of the following (a or b):
   a. At least 10% of the member's body surface area (BSA);
   b. Hands, feet, face, neck, scalp, genitals/groin, and/or intertriginous areas;
2. Prescribed by or in consultation with a dermatologist or allergist;
3. Age ≥ 12 years;
4. Failure of both of the following (a and b), unless contraindicated or clinically significant adverse effects are experienced:
   a. Two formulary medium to very high potency topical corticosteroids, each used for ≥ 2 weeks;
   b. One non-steroidal topical therapy* used for ≥ 4 weeks: topical calcineurin inhibitor (e.g., tacrolimus 0.03% ointment, pimecrolimus 1% cream) or Eucrisa®;
      **These agents may require prior authorization*
5. Rivoq is not prescribed concurrently with another biologic medication (e.g., Adbry®, Dupixent®) or a JAK inhibitor (e.g., Olumiant®, Cibinqo®, Opzelura™);
6. Dose does not exceed one of the following (a or b):
   a. Both of the following (i and ii):
      i. 15 mg per day;
      ii. 1 tablet per day;
   b. Medical justification supports inadequate response to 15 mg daily and both of the following (i and ii):
      i. 30 mg per day;
      ii. 1 tablet per day.

Approval duration: 6 months

D. Axial Spondyloarthritis (must meet all)**:**

1. Diagnosis of AS or nr-axSpA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Failure of at least TWO non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for ≥ 4 weeks unless clinically significant adverse effects are experienced or all are contraindicated;
5. For AS, member meets ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c, *see Appendix D*):
   a. Failure of one adalimumab product (e.g. *Hadlima™, Yusimry™, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), unless the member has had a history of failure of two TNF blockers;

b. Failure of Taltz;
c. If member has not responded or is intolerant to one or more TNF blockers, Xeljanz/Xeljanz XR, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

**Prior authorization may be required for adalimumab products, Xeljanz/Xeljanz XR, and Taltz*

6. For nr-axSpA: Failure of Taltz*, used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Taltz*
7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. Dose does not exceed both of the following (a and b):
   a. 15 mg per day;
   b. 1 tablet per day.

Approval duration: 6 months

E. 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 H*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
6. Member meets BOTH of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a and b, *see Appendix D*):
   a. One of the following (i or ii):
      i. Failure of one adalimumab product (e.g. *Hadlima™, Yusimry™, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), used for ≥ 3 consecutive months;
      ii. History of failure of two TNF blockers;
   b. If member has had a history of failure of two TNF blockers, then failure of Zeposia®;

   **Prior authorization may be required for adalimumab products and Zeposia*
7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. Request meets one of the following (a or b):
   a. For induction (both i and ii):
      i. 45 mg once daily for 8 weeks;
      ii. 1 tablet once daily for 8 weeks;
   b. For maintenance (both i and ii):
      i. 15 mg once daily;
      ii. 1 tablet once daily.

Approval duration: 6 months

F. Crohn's Disease (must meet all)**:**

1. Diagnosis of CD;

2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], methotrexate [MTX]) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Medical justification supports inability to use immunomodulators (*see Appendix I*);
5. Member meets one of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a or b, *see Appendix D*):*
   a. Failure of one adalimumab product (e.g. *Hadlima™, Yusimry™, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), used for ≥ 3 consecutive months;
   b. History of failure of two TNF blockers;

   **Prior authorization may be required for adalimumab products*
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Request meets one of the following (a or b):
   a. For induction (both i and ii):
      i. 45 mg once daily for 12 weeks;
      ii. 1 tablet once daily for 8 weeks;
   b. Medical justification supports inadequate response to 15 mg daily and both of the following (i and ii):
      i. 30 mg per day;
      ii. 1 tablet per day.

Approval duration: 6 months

G. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. A decrease in CDAI (*see Appendix F*) or RAPID3 (*see Appendix G*) score from baseline;
   b. 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;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
4. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 15 mg per day;
   b. 1 tablet per day.

Approval duration: 12 months

B. Atopic Dermatitis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by, including but not limited to, reduction in itching and scratching;
3. Rinvoq is not prescribed concurrently with another biologic medication (e.g., Adbry, Dupixent) or a JAK inhibitor (e.g., Olumiant, Cibinqo, Opzelura);
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Both of the following (i and ii):
      i. 15 mg per day;
      ii. 1 tablet per day;
   b. Medical justification supports inadequate response to 15 mg daily and both of the following (i and ii):
      i. 30 mg per day;
      ii. 1 tablet per day.

Approval duration: 12 months

C. All Other Indications (must meet all)**:**

1. Member meets one of the following (a or b):

a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. Member is responding positively to therapy;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
4. If request is for a dose increase, new dose does not exceed (a or b):
   a. For PsA, UC, AS, nr-axSpA: both of the following (i and ii):
      i. 15 mg per day;
      ii. 1 tablet per day;
   b. For refractory, severe, or extensive UC or CD: both of the following (i and ii):
      i. 30 mg per day;
      ii. 1 tablet per day.

Approval duration: 12 months

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 policy – CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Combination use with biological disease-modifying antirheumatic drugs (bDMARDs) or potent immunosuppressants, including but not limited to any tumor necrosis factor (TNF) antagonists [e.g., Cimzia®, Enbrel®, Humira® and its biosimilars, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [e.g., Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL-23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Xeljanz®/Xeljanz® XR, Cibinqo™, Olumiant™, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®,

Riabni™, Ruxience™, Truxima®, Rituxan Hycela®], selective co-stimulation modulators [Orencia®], and integrin receptor antagonists [Entyvio®] because of the additive immunosuppression, increased risk of neutropenia, as well as increased risk of serious infections.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AS: ankylosing spondylitis
CD: Crohn's disease
CDAI: clinical disease activity index
DMARD: disease-modifying antirheumatic drug
FDA: Food and Drug Administration
JAKi: Janus kinase inhibitors
MTX: methotrexate
nr-axSpA: non-radiographic axial spondyloarthritis
PsA: psoriatic arthritis
RA: rheumatoid arthritis
RAPID3: routine assessment of patient index data 3

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 **CD** 1.5 – 2 mg/kg/day PO	3 mg/kg/day
corticosteroids	**UC*** Prednisone 40 mg – 60 mg PO QD, then taper dose by 5 to 10 mg/week Budesonide (Uceris®) 9 mg PO QAM for up to 8 weeks **CD*** *Adult:* prednisone 40 mg – 60 mg PO QD for 1 to 2 weeks, then taper daily dose by 5 mg weekly until 20 mg PO QD, and then continue with 2.5 – 5 mg decrements weekly or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC®) 6 – 9 mg PO QD *Pediatric:*	Various

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Prednisone 1 to 2 mg/kg/day PO QD	
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	RA: 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** Initial dose (for low risk hepatotoxicity or myelosuppression): 100 mg PO QD for 3 days Maintenance dose: 20 mg PO QD	20 mg/day
6-mercaptopurine (Purixan®)	**CD*** 50 mg PO QD or 0.75 – 1.5 mg/kg/day PO	1.5 mg/kg/day
methotrexate (Trexall®, Otrexup™, Rasuvo®, RediTrex®, Xatmep™, Rheumatrex®)	**RA** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week **CD*** 15 – 25 mg/week IM or SC	30 mg/week
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS** Varies	Varies
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day
Ridaura® (auranofin)	**RA** 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine®)	**RA** Initial dose: 500 mg to 1,000 mg PO QD for the first week. Increase the daily dose by 500 mg	3 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	each week up to a maintenance dose of 2 g/day. Maintenance dose: 2 g/day PO in divided doses	
Actemra® (tocilizumab)	**RA** IV: 4 mg/kg every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response SC: Weight < 100 kg: 162 mg SC every other week, followed by an increase to every week based on clinical response Weight ≥ 100 kg: 162 mg SC every week	IV: 800 mg every 4 weeks SC: 162 mg every week
Cimzia® (certolizumab)	**nr-axSpA** Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 200 mg SC every other week (or 400 mg SC every 4 weeks) **CD** Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 400 mg SC every 4 weeks	400 mg every 4 weeks
Hadlima (adalimumab-bwwd), Yusimry (adalimumab-aqvh), adalimumab-adaz (Hyrimoz®), adalimumab-fkjp (Hulio®), adalimumab-adbm (Cyltezo®)	**UC** Initial dose: 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: 40 mg SC every other week starting on Day 29 **CD** Initial dose: 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: 40 mg SC every other week starting on Day 29	40 mg every other week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	RA, AS, PsA 40 mg SC every other week	
Taltz® (ixekizumab)	**AS, nr-axSpA, PsA** Initial dose: 160 mg (two 80 mg injections) SC at week 0 Maintenance dose: 80 mg SC every 4 weeks	80 mg every 4 weeks
Xeljanz® (tofacitinib)	**AS, PsA, RA** 5 mg PO BID	10 mg/day
Xeljanz XR® (tofacitinib extended-release)	**AS, PsA, RA** 11 mg PO QD	11 mg/day
Very High Potency Topical Corticosteroids		
augmented betamethasone 0.05% (Diprolene® AF) cream, ointment, gel, lotion	**AD** Apply topically to the affected area(s) BID	Varies
clobetasol propionate 0.05% (Temovate®) cream, ointment, gel, solution		
diflorasone diacetate 0.05% (Maxiflor®, Psorcon E®) cream, ointment		
halobetasol propionate 0.05% (Ultravate®) cream, ointment		
High Potency Topical Corticosteroids		
augmented betamethasone 0.05% (Diprolene® AF) cream, ointment, gel, lotion	**AD** Apply topically to the affected area(s) BID	Varies
diflorasone 0.05% (Florone®, Florone E®,		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Maxiflor®,Psorcon E®) cream		
fluocinonide acetonide 0.05% (Lidex®, Lidex E®) cream, ointment, gel, solution		
triamcinolone acetonide 0.5% (Aristocort®, Kenalog®) cream, ointment		
Medium Potency Topical Corticosteroids		
desoximetasone 0.05% (Topicort ®) cream, ointment, gel	**AD** Apply topically to the affected area(s) BID	Varies
fluocinolone acetonide 0.025% (Synalar®) cream, ointment		
mometasone 0.1% (Elocon®) cream, ointment, lotion		
triamcinolone acetonide 0.025%, 0.1% (Aristocort®, Kenalog®) cream, ointment		
Low Potency Topical Corticosteroids		
alclometasone 0.05% (Aclovate®) cream, ointment	**AD** Apply topically to the affected area(s) BID	Varies
desonide 0.05% (Desowen®) cream, ointment, lotion		
fluocinolone acetonide 0.01% (Synalar®) solution		
hydrocortisone 2.5% (Hytone®) cream, ointment		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Other Classes of Agents		
tacrolimus (Protopic®), pimecrolimus (Elidel®)	**AD** Children ≥ 2 years and adults: Apply a thin layer topically to affected skin BID. Treatment should be discontinued if resolution of disease occurs.	Varies
Eucrisa® (crisaborole)	**AD** Apply to the affected areas BID	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): known hypersensitivity to upadacitinib or any of the excipients in Rinvoq
- Boxed warning(s): serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis

Appendix D: General Information

- Definition of MTX or DMARD Failure
  - 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 ESR/CRP levels
  - Improvements in activities of daily living
- Nr-axSpA: guideline recommendations are largely extrapolated from evidence in AS.
- TNF blockers:
  - Etanercept (Enbrel®), adalimumab (Humira®) and its biosimilars, infliximab (Remicade®) and its biosimilars (Avsola™, Renflexis™, Inflectra®), certolizumab pegol (Cimzia®), and golimumab (Simponi®, Simponi Aria®).

Appendix E: 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 F: 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 G: 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 H: 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

Appendix I: Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:
  - Inability to induce short-term symptomatic remission with a 3-month trial of systemic glucocorticoids
  - High-risk factors for intestinal complications may include:
    - Initial extensive ileal, ileocolonic, or proximal GI involvement
    - Initial extensive perianal/severe rectal disease
    - Fistulizing disease (e.g., perianal, enterocutaneous, and rectovaginal fistulas)
    - Deep ulcerations
    - Penetrating, structuringg or stenosis disease and/or phenotype
    - Intestinal obstruction or abscess

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
AS, nr-axSpA, RA, PsA	15 mg PO QD	15 mg/day
AD	• Age ≥ 12 years and ≥ 40 kg but < 65 years: 15 mg PO QD; if an adequate response is not achieved, consider increasing the dosage to 30 mg PO QD • Age ≥ 65 years: 15 mg PO QD	• Age ≥ 12 years and ≥ 40 kg but < 65 years: 30 mg/day • Age ≥ 65 years: 15 mg/day
UC	• Induction: 45 mg PO Q for 8 weeks • Maintenance: 15 mg PO QD. A dosage of 30 mg PO QD may be considered for patients with refractory, severe, or extensive disease.	30 mg/day
CD	• Induction: 45 mg PO Q for 12 weeks • Maintenance: 15 mg PO QD. A dosage of 30 mg PO QD may be considered for patients with refractory, severe, or extensive disease.	30 mg/day

VI. Product Availability

Tablets, extended-release: 15 mg, 30 mg, 45 mg

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.15.19	11.19
Removed HIM-TBD line of business; updated preferred redirections based on SDC recommendation and prior clinical guidance: for RA, removed redirection to adalimumab and added redirection to 2 of 3 agents (Enbrel, Kevzara, Xeljanz/Xeljanz XR).	12.13.19	
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; references reviewed and updated.	04.29.20	05.20
Revised typo in Appendix E from "normal ESR" to "abnormal ESR" for a point gained for ACR Classification Criteria.	11.22.20	
Added criteria for RAPID3 assessment for RA given limited in-person visits during COVID-19 pandemic, updated appendices.	11.24.20	02.21
2Q 2021 annual review: added combination of bDMARDs under Section III; updated CDAI table with ">" to prevent overlap in classification of severity; references reviewed and updated.	02.23.21	05.21
Per August SDC and prior clinical guidance, for RA added Actemra to redirect options and modified to require a trial of all; for Xeljanz redirection requirements added bypass for members with cardiovascular risk and qualified redirection to apply only for member that has not responded or is intolerant to one or more TNF blockers; added Legacy WellCare line of business to policy (WCG.CP.PHAR.443 to be retired).	08.25.21	11.21
2Q 2022 annual review: for RA, added redirection to Olumiant per February SDC; criteria added for new FDA indications: psoriatric arthritis, atopic dermatitis; revised Rinvoq's place in therapy after TNFi for RA and PsA per FDA labeling; RT4: added newly FDA-approved indications for UC and AS; reiterated requirement against	05.02.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated.		
RT4: revised lower age limit for AD from 18 to 12 years per PI. Template changes applied to other diagnoses/indications and continued therapy section.	09.15.22	
RT4: criteria added for new FDA indication: nr-axSpA.	10.31.22	
Per February SDC, added Amjevita as an alternative option to Humira for UC.	02.13.23	
2Q 2023 annual review: for RA, PsA, AS, and UC, added TNFi criteria to allow bypass if member has had history of failure of two TNF blockers; updated off-label dosing for Appendix B; references reviewed and updated.	02.10.23	05.23
RT4: criteria added for new FDA indication: Crohn's disease.	05.25.23	
Per July SDC: for PsA and RA, removed criteria requiring use of Enbrel; for AS, removed criteria requiring use of Cimzia and Enbrel; for nr-axSpA, removed redirection to Cimzia; for UC, removed criteria requiring use of Simponi, Humira, and Amjevita; for PsA, RA, AS, UC, CD, added criteria requiring use of one adalimumab product and stating Yusimry, Hadlima, unbranded adalimumab-fkjp, and unbranded adalimumab-adaz as preferred; updated Appendix B with relevant therapeutic alternatives.	07.25.23	
Per December SDC, added adalimumab-adbm to listed examples of preferred adalimumab products; for RA removed redirection to Kevzara and Olumiant. For AD initial criteria, removed systemic immunosuppressant therapy step criterion per updated guideline and competitor analysis; for Appendix B, removed systemic immunosuppressant therapy therapeutic alternatives.	12.06.23	02.24

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.