

Clinical Policy: Upadacitinib (Rinvoq, Rinvoq LQ)

Reference Number: MDN.CP.PHAR.443

Effective Date: 12.01.19

Last Review Date: 12.3.24

Line of Business: Meridian IL Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Upadacitinib (Rinvoq[®], Rinvoq LQ[®]) is a Janus kinase (JAK) inhibitor.

FDA Approved Indication(s)

Rinvoq and Rinvoq LQ are indicated for treatment of:

- Adults and pediatric patients 2 years of age and older with active psoriatic arthritis who have had an inadequate response or intolerance to one or more TNF blockers.
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (pJIA) who have had an inadequate response or intolerance to one or more TNF blockers.

Rinvoq is also 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 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 intolerance 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/Rinvoq LQ 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/Rinvoq LQ are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

CLINICAL POLICY

Upadacitinib

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. Request is for Rinvoq; unless a, b, or c:
 - a. Documentation why member cannot take solid dosage form (age, g-tube, etc);
 - b. Oral-motor difficulties;
 - c. Dysphagia;
5. 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;
6. Failure of TWO of the following, each used for ≥ 3 consecutive months, unless the member has had a history of failure of two TNF blockers clinically significant adverse effects are experienced or all are contraindicated (a, b, c, and d):
 - a. Cimzia[®];
 - b. Enbrel[®];
 - c. Humira[®];
 - d. Xeljanz[®]/Xeljanz XR[®];

**Prior authorization may be required for Cimzia, Enbrel, Humira, and Xeljanz/Xeljanz XR*
7. 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*);
8. 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);
9. Dose does not exceed 15 mg (one 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 ≥ 2 years;
4. Request is for Rinvoq; unless a, b, or c:
 - a. Documentation why member cannot take solid dosage form (age, g-tube, etc);
 - b. Oral-motor difficulties;
 - c. Dysphagia;
5. Failure of TWO of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c):

CLINICAL POLICY

Upadacitinib

- a. Cimzia®;
 - b. Enbrel®;
 - 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 Cimzia, Enbrel, and Xeljanz/Xeljanz XR*
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. Dose does not exceed one of the following (a or b):
- a. Age \geq 18 years: Both of the following (i and ii) (*Rinvoq*):
 - i. 15 mg per day;
 - ii. 1 tablet per day;
 - b. Age \geq 2 to < 18 years: One of the following (i, ii, or iii):
 - i. Weight 10 kg to < 20 kg: 6 mg per day (*Rinvoq LQ*);
 - ii. Weight 20 kg to < 30 kg: 8 mg per day (*Rinvoq LQ*);
 - iii. Weight \geq 30 kg, one of the following (1 or 2):
 - 1) 12 mg per day (*Rinvoq LQ*);
 - 2) Both of the following (a and b) (*Rinvoq*):
 - 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 \geq 12 years;
 4. Request is for Rinvoq; unless a, b, or c:
 - a. Documentation why member cannot take solid dosage form (age, g-tube, etc);
 - b. Oral-motor difficulties;
 - c. Dysphagia;
 5. Failure of all of the following (a, b, and c), unless contraindicated or clinically significant adverse effects are experienced:
 - a. Two formulary medium to very high potency topical corticosteroids, each used for \geq 2 weeks;
 - b. One non-steroidal topical therapy* used for \geq 4 weeks: topical calcineurin inhibitor (e.g., tacrolimus ointment, pimecrolimus cream) or Eucrisa®;
**These agents may require prior authorization*
 - c. Dupixent* used for \geq 3 consecutive months
**Dupixent may require prior authorization*
 6. Rinvoq is not prescribed concurrently with another biologic medication (e.g., Adbry®, Dupixent®) or a JAK inhibitor (e.g., Olumiant®, Cibinco®, Opzelura™);
 7. Dose does not exceed one of the following (a or b):

CLINICAL POLICY

Upadacitinib

- a. 15 mg (1 tab) per day;
- b. Medical justification supports inadequate response to 15 mg daily and dose is 30 mg (1 tab) 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 \geq 18 years;
4. Request is for Rinvoq; unless a, b, or c:
 - a. Documentation why member cannot take solid dosage form (age, g-tube, etc);
 - b. Oral-motor difficulties;
 - c. Dysphagia;
5. Failure of at least TWO non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for \geq 4 weeks unless clinically significant adverse effects are experienced or all are contraindicated;
6. For AS: Failure of TWO of the following, each used for \geq 3 consecutive months, unless the member has had a history of failure of two TNF blockers, clinically significant adverse effects are experienced or all are contraindicated (a, b, c, and d):
 - a. Cimzia[®];
 - b. Enbrel[®];
 - c. Humira[®];
 - d. Xeljanz[®]/Xeljanz XR[®];

**Prior authorization may be required for Cimzia, Enbrel, and Xeljanz/Xeljanz XR*
7. For nr-axSpA: Failure of the following, used for \geq 3 consecutive months, unless clinically significant adverse effects are experienced for both are contraindicated: Cimzia;
8. 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);
9. Dose does not exceed 15 mg (one 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. Request is for Rinvoq; unless a, b, or c:
 - a. Documentation why member cannot take solid dosage form (age, g-tube, etc);
 - b. Oral-motor difficulties;
 - c. Dysphagia;
4. Age \geq 18 years;
5. Documentation of a Mayo Score \geq 6 (see Appendix H);
6. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
7. Failure of Humira[®], used for \geq 3 consecutive months, unless clinically significant adverse effects are experienced or contraindicated

CLINICAL POLICY

Upadacitinib

8. 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);
9. Dose meets the following:
 - a. For induction: 45 mg (one tablet) once daily for 8 weeks;
 - b. For maintenance: 15 mg (one tablet) once daily or medical justification supports inadequate response to 15 mg daily and dose is 30 mg (1 tab) per day.

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. Request is for Rinvoq; unless a, b, or c:
 - a. Documentation why member cannot take solid dosage form (age, g-tube, etc);
 - b. Oral-motor difficulties;
 - c. Dysphagia;
3. Age \geq 18 years;
4. Member meets one of the following (a or b):
 - a. Failure of a \geq 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 Humira used for \geq 3 consecutive months;
 - b. History of failure of two TNF blockers;

**Prior authorization may be required for adalimumab*
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. Dose meets the following:
 - a. For induction: 45 mg (1 tablet) once daily for 12 weeks;
 - b. For maintenance: 15 mg (one tablet) once daily or medical justification supports inadequate response to 15 mg daily and dose is 30mg (1 tab) per day.

Approval duration: 6 months

G. Polyarticular Juvenile Idiopathic Arthritis (must meet all):

1. Diagnosis of PJIA* as evidenced by \geq 5 joints with active arthritis;
**Overlap of diagnosis exists in children with JIA and non-systemic polyarthritis, which may include children from ILAR JIA categories of enthesitis-related arthritis*
2. Prescribed by or in consultation with a rheumatologist;
3. Age \geq 2 years;
4. Documented baseline 10-joint clinical juvenile arthritis disease activity score (cJADAS-10) (*see Appendix J*);
5. Member meets one of the following (a, b, c, or d):

CLINICAL POLICY

Upadacitinib

- a. Failure of a ≥ 3 consecutive month trial of 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 leflunomide or sulfasalazine at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
 - c. For sacroiliitis/axial spine involvement (i.e., spine, hip), failure of a ≥ 4 week trial of an NSAID at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
 - d. Documented presence of high disease activity as evidenced by a cJADAS-10 > 8.5 (*see Appendix J*);
6. Failure of ALL* of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated (a, b, and c, *see Appendix D*):
- a. Humira[®];
 - b. If member has not responded or is intolerant to one or more TNF blockers, Xeljanz, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;
- *Prior authorization may be required for Humira and Xeljanz*
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 one of the following (a, b, or c):
- a. Weight 10 kg to < 20 kg: 6 mg per day (*Rinvoq LQ*);
 - b. Weight 20 kg to < 30 kg: 8 mg per day (*Rinvoq LQ*);
 - c. Weight ≥ 30 kg, one of the following (i or ii):
 - i. 12 mg per day (*Rinvoq LQ*);
 - ii. Both of the following (1 and 2) (*Rinvoq*):
 - 1) 15 mg per day;
 - 2) 1 tablet per day.

Approval duration: 6 months

H. 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.

CLINICAL POLICY

Upadacitinib

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. Request is for Rinvoq;
3. 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;
4. 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);
5. If request is for a dose increase, new dose does not exceed 15 mg (one tablet) per day.

Approval duration: 12 months

B. Atopic Dermatitis (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request is for Rinvoq;
3. Member is responding positively to therapy as evidenced by, including but not limited to, reduction in itching and scratching;
4. Rinvoq is not prescribed concurrently with another biologic medication (e.g., Adbry®, Dupixent®) or a JAK inhibitor (e.g., Olumiant®, Cibinqo®, Opzelura™);
5. 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 dose is both 30 mg (1 tab) 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;

CLINICAL POLICY

Upadacitinib

- 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. For CD, UC, AS, nr-axSpA: Request is for Rinvoq;
3. For CD, UC, AS, nr-axSpA, PsA: Member is responding positively to therapy;
4. For pJIA: Member is responding positively to therapy as evidenced by a decrease in cJADAS-10 from baseline (*see Appendix J*);
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. 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*);
5. If request is for a dose increase, new dose does not exceed (a, b, c, or d):
 - a. For UC, AS, nr-axSpA: Both of the following (i and ii) (*Rinvoq*):
 - 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) (*Rinvoq*):
 - i. 30 mg per day;
 - ii. 1 tablet per day;
 - c. For PsA: One of the following (i or ii):
 - i. Age \geq 18 years: Both of the following (1 and 2) (*Rinvoq*):
 - 1) 15 mg per day;
 - 2) 1 tablet per day;
 - ii. Age \geq 2 to < 18 years: One of the following (1, 2, or 3):
 - 1) Weight 10 kg to < 20 kg: 6 mg per day (*Rinvoq LQ*);
 - 2) Weight 20 kg to < 30 kg: 8 mg per day (*Rinvoq LQ*);
 - 3) Weight \geq 30 kg: One of the following (a or b):
 - a) 12 mg per day (*Rinvoq LQ*);
 - b) Both of the following (i and ii) (*Rinvoq*):
 - i) 15 mg per day;
 - ii) 1 tablet per day;
 - d. For pJIA: One of the following (i, ii, or iii):
 - i. Weight 10 kg to < 20 kg: 6 mg per day (*Rinvoq LQ*);
 - ii. Weight 20 kg to < 30 kg: 8 mg per day (*Rinvoq LQ*);
 - iii. Weight \geq 30 kg, one of the following (1 or 2):
 - 1) 12 mg per day (*Rinvoq LQ*);
 - 2) Both of the following (a and b) (*Rinvoq*):
 - a) 15 mg per day;
 - b) 1 tablet per day.

Approval duration: 12 months

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

CLINICAL POLICY

Upadacitinib

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, Remicade[®] and its biosimilars (Avsola[™], Inflectra[™], Renflexis[™], Zymfentra[®]), Simponi[®]], interleukin agents [e.g., Actemra[®] (IL-6RA), Arcalyst[®] (IL-1 blocker), Bimzelx[®] (IL-17A and F antagonist), Cosentyx[®] (IL-17A inhibitor), Ilaris[®] (IL-1 blocker), Ilumya[™] (IL-23 inhibitor), Kevzara[®] (IL-6RA), Kineret[®] (IL-1RA), Omvoh[™] (IL-23 antagonist), Siliq[™] (IL-17RA), Skyrizi[™] (IL-23 inhibitor), Stelara[®] (IL-12/23 inhibitor), Taltz[®] (IL-17A inhibitor), Tofidence[™] (IL-6), Tremfya[®] (IL-23 inhibitor), Wezlana[™] (IL-12/23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Cibinqo[™], Olumiant[™], Rinvoq[™], Xeljanz[®]/Xeljanz[®] XR,], anti-CD20 monoclonal antibodies [Rituxan[®] and its biosimilars (Riabni[™], Ruxience[™], Truxima[®]), Rituxan Hycela[®]], selective co-stimulation modulators [Orencia[®]], integrin receptor antagonists [Entyvio[®]], tyrosine kinase 2 inhibitors [Sotyktu[™]], and sphingosine 1-phosphate receptor modulator [Velsipity[™]] 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

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

CLINICAL POLICY

Upadacitinib

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* <i>Adult:</i> 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 <i>Pediatric:</i> Prednisone 1 to 2 mg/kg/day PO QD	Various
Cuprimine [®] (d-penicillamine)	RA* <u>Initial dose:</u> 125 or 250 mg PO QD <u>Maintenance dose:</u> 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* <u>Initial dose:</u> 400 – 600 mg/day PO QD <u>Maintenance dose:</u> 200 – 400 mg/day PO QD	600 mg/day

CLINICAL POLICY
Upadacitinib

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
leflunomide (Arava [®])	RA <u>Initial dose (for low risk hepatotoxicity or myelosuppression):</u> 100 mg PO QD for 3 days <u>Maintenance dose:</u> 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 <u>Initial dose:</u> 500 mg to 1,000 mg PO QD for the first week. Increase the daily dose by 500 mg each week up to a maintenance dose of 2 g/day. <u>Maintenance dose:</u> 2 g/day PO in divided doses	3 g/day
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 [®]	nr-axSpA	400 mg every 4 weeks

CLINICAL POLICY
Upadacitinib

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(certolizumab)	<p><u>Initial dose:</u> 400 mg SC at 0, 2, and 4 weeks</p> <p><u>Maintenance dose:</u> 200 mg SC every other week (or 400 mg SC every 4 weeks)</p> <p>CD</p> <p><u>Initial dose:</u> 400 mg SC at 0, 2, and 4 weeks</p> <p><u>Maintenance dose:</u> 400 mg SC every 4 weeks</p>	
<p>Hadlima (adalimumab-bwwd), Yusimry (adalimumab-aqvh), adalimumab-adaz (Hyrimoz[®]), adalimumab-fkjp (Hulio[®]), adalimumab-adbm (Cyltezo[®])</p>	<p>UC</p> <p><u>Initial dose:</u> 160 mg SC on Day 1, then 80 mg SC on Day 15</p> <p><u>Maintenance dose:</u> 40 mg SC every other week starting on Day 29</p> <p>CD</p> <p><u>Initial dose:</u> 160 mg SC on Day 1, then 80 mg SC on Day 15</p> <p><u>Maintenance dose:</u> 40 mg SC every other week starting on Day 29</p> <p>RA, AS, PsA 40 mg SC every other week</p>	40 mg every other week
<p>Taltz[®] (ixekizumab)</p>	<p>AS, nr-axSpA, PsA</p> <p><u>Initial dose:</u> 160 mg (two 80 mg injections) SC at week 0</p> <p><u>Maintenance dose:</u> 80 mg SC every 4 weeks</p>	80 mg every 4 weeks
<p>Xeljanz[®] (tofacitinib)</p>	<p>AS, PsA, RA 5 mg PO BID</p>	10 mg/day
<p>Xeljanz XR[®] (tofacitinib extended-release)</p>	<p>AS, PsA, RA 11 mg PO QD</p>	11 mg/day
Very High Potency Topical Corticosteroids		

CLINICAL POLICY

Upadacitinib

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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 [®] , Maxiflor [®] , Psorcon E [®]) cream		
fluocinonide acetone 0.05% (Lidex [®] , Lidex E [®]) cream, ointment, gel, solution		
triamcinolone acetone 0.5% (Aristocort [®] , Kenalog [®]) cream, ointment		
Medium Potency Topical Corticosteroids		
desoximetasone 0.05% (Topicort [®])	AD	Varies

CLINICAL POLICY
Upadacitinib

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cream, ointment, gel	Apply topically to the affected area(s) BID	
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		
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

CLINICAL POLICY

Upadacitinib

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/Rinvoq LQ
- 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
 - TNF blockers:
 - Etanercept (Enbrel[®]), adalimumab (Humira[®]), adalimumab-atto (Amjevita[™]), infliximab (Remicade[®]) and infliximab 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: $< 3 \times$ upper limit of normal	2
	High positive RF or high positive ACPA * High: $\geq 3 \times$ upper limit of normal	3

CLINICAL POLICY

Upadacitinib

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
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

CLINICAL POLICY

Upadacitinib

Score	Decoding
>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, structuring or stenosis disease and/or phenotype
 - Intestinal obstruction or abscess

Appendix J: Clinical Juvenile Arthritis Disease Activity Score Based on 10 Joints (cJADAS-10)

The cJADAS10 is a continuous disease activity score specific to JIA and consisting of the following three parameters totaling a maximum of 30 points:

- Physician’s global assessment of disease activity measured on a 0-10 visual analog scale (VAS), where 0 = no activity and 10 = maximum activity;
- Parent global assessment of well-being measured on a 0-10 VAS, where 0 = very well and 10 = very poor;
- Count of joints with active disease to a maximum count of 10 active joints*

*ACR definition of active joint: presence of swelling (not due to currently inactive synovitis or to bony enlargement) or, if swelling is not present, limitation of motion accompanied by pain, tenderness, or both

cJADAS-10	Disease state interpretation
≤ 1	Inactive disease
1.1 to 2.5	Low disease activity
2.51 to 8.5	Moderate disease activity
> 8.5	High disease activity

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Upadacitinib (Rinvoq)	AS, nr-axSpA, RA	15 mg PO QD	15 mg/day
	AD	<u>Age ≥ 12 years and ≥ 40 kg but < 65 years:</u> 15 mg PO QD; if an adequate response is not achieved, consider increasing the dosage to 30 mg PO QD <u>Age ≥ 65 years:</u> 15 mg PO QD	<u>Age ≥ 12 years and ≥ 40 kg but < 65 years:</u> 30 mg/day <u>Age ≥ 65 years:</u> 15 mg/day
	UC	<u>Induction:</u> 45 mg PO Q for 8 weeks	30 mg/day

CLINICAL POLICY

Upadacitinib

Drug Name	Indication	Dosing Regimen	Maximum Dose
		<u>Maintenance</u> : 15 mg PO QD. A dosage of 30 mg PO QD may be considered for patients with refractory, severe, or extensive disease.	
	CD	<u>Induction</u> : 45 mg PO Q for 12 weeks <u>Maintenance</u> : 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
	PsA	<u>Age ≥ 18 years</u> : 15 mg PO QD <u>Age ≥ 2 years but < 18 years</u> : Weight ≥ 30 kg: 15 mg PO QD	15 mg/day
	pJIA	<u>Age ≥ 2 years</u> : Weight ≥ 30 kg: 15 mg PO QD	15 mg/day
Upadacitinib (Rinvoq LQ)	PsA	<u>Age ≥ 2 years but < 18 years</u> : <ul style="list-style-type: none"> • Weight 10 kg to < 20 kg: 3 mg (3 mL oral solution) PO BID • Weight 20 kg to < 30 kg: 4 mg (4 mL oral solution) PO BID • Weight ≥ 30 kg: 6 mg (6 mL oral solution) PO BID 	12 mg/day
	pJIA	<u>Age ≥ 2 years</u> : <ul style="list-style-type: none"> • Weight 10 kg to < 20 kg: 3 mg (3 mL oral solution) PO BID • Weight 20 kg to < 30 kg: 4 mg (4 mL oral solution) PO BID • Weight ≥ 30 kg: 6 mg (6 mL oral solution) PO BID 	12 mg/day

VI. Product Availability

Drug Name	Availability
Upadacitinib (Rinvoq)	Tablets, extended-release: 15 mg, 30 mg, 45 mg
Upadacitinib (Rinvoq LQ)	Oral solution: 1 mg/mL

VII. References

CLINICAL POLICY

Upadacitinib

1. Rinvoq/Rinvoq LQ Prescribing Information. North Chicago, IL: AbbVie Inc.; April 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218347s000lbl.pdf. Accessed May 10, 2024.
2. Singh JA., Saag KG, Bridges SL, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Care & Research*. 68: 1–25. doi:10.1002/acr.22783.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed January 11, 2021.
4. 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.
5. 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.
6. Wollenberg A, Christen-Zäch S, Taieb A, et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol*. 2020 Dec;34(12):2717-2744.
7. Eichenfield F, Tom WL, Chamlin SL, et al. Guidelines of Care for the Management of Atopic Dematitis. *J Am Acad Dermatol*. 2014 February; 70(2): 338–351.
8. Ward MM, Deodhar A, Gensler L, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of anklyosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis & Rheumatology*. 2019; 71(10):1599-1613. DOI 10.1002/ART.41042.

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	08.25.21	11.21

CLINICAL POLICY

Upadacitinib

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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).		
Criteria added for new FDA indications: psoriatic arthritis, atopic dermatitis; added newly FDA approved indications for UC and AS; reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated.	08.12.22	
RT4: criteria added for new FDA indication: nr-axSpA; Template changes applied to other diagnoses/indications and continued therapy section; references reviewed and updated	11.30.22	
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.	4.22.23	
2Q 2024 annual review: removed nr-axSpA supplemental guideline information in Appendix D; added Bimzelx, Zymfentra, Omvoh, Wezlana, Sotyktu, Tofidence, and Velsipity to section III.B; For AD initial criteria, removed systemic immunosuppressant therapy step criterion per updated guideline and competitor analysis; for Appendix B; criteria added for new FDA indication: Crohn's disease references reviewed and updated.	5.16.24	
Appendix I and J added	7.12.24	
RT4: for PsA, updated criteria to reflect pediatric extension to 2 years and older; added new FDA approved pJIA indication; for PsA and pJIA, added new oral solution dosage form [Rinvoq LQ].	12.3.24	
Added clarifier of "For AS" to 1.D.6	2.10.25	

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.

CLINICAL POLICY

Upadacitinib

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.

©2019 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.