

CLINICAL POLICY

Infliximab, Infliximab-dyyb, Infliximab-abda



Clinical Policy: Infliximab (Remicade, Inflectra, Renflexis, Avsola, Zymfentra)

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Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

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

Description

Infliximab (Remicade[®]) and its biosimilars, infliximab-axxq (Avsola[™]), infliximab-dyyb (Inflectra[®]), infliximab-dyyb (Inflectra[®], Zymfentra[®]), and infliximab-abda (Renflexis[™]), are tumor necrosis factor (TNF) blockers.

FDA Approved Indication(s)

Remicade/unbranded Remicade, Avsola, Inflectra and Renflexis are indicated for the treatment of:

- Crohn's Disease (CD):
 - Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active CD who have had an inadequate response to conventional therapy
 - Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD
- Pediatric CD:
 - Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active CD who have had an inadequate response to conventional therapy
- Ulcerative Colitis (UC):
 - Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active UC who have had an inadequate response to conventional therapy
- Pediatric UC:
 - Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active UC who have had an inadequate response to conventional therapy
- Rheumatoid Arthritis (RA):
 - Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active RA, in combination with methotrexate (MTX)
- Ankylosing Spondylitis (AS):
 - Reducing signs and symptoms in patients with active AS
- Psoriatic Arthritis (PsA):

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- Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with PsA
- Plaque Psoriasis (PsO):
 - Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) PsO who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. Infliximab should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician

Zymfentra is indicated for the treatment of:

- Moderate to severely active UC following treatment with an infliximab product administered intravenously
- Moderate to severely active CD following treatment with an infliximab product administered intravenously

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 Remicade, Avsola, Inflectra, Zymfentra, and Renflexis are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. Crohn's Disease** (must meet all):

1. Diagnosis of CD;
2. Prescribed by or in consultation with a gastroenterologist;
3. Member meets one of the following (a or b):
 - a. Age ≥ 6 years and meets one of the following (i or ii)
 - i. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], MTX) at up to maximally indicated doses, unless contraindicated, clinically significant adverse effects are experienced, or medical justification supports inability to use immunomodulators (*see Appendix E*);
 - ii. Failure of a ≥ 3 consecutive month trial of adalimumab Adalimumab-adbm and Simlandi® are *preferred*)
 - b. Age ≥ 18 years: Failure of a ≥ 3 consecutive month trial of adalimumab Adalimumab-adbm and Simlandi® are *preferred*) and certolizumab (*Cimzia is preferred*), unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for Zymfentra, provider attestation that member meets all of the following (a, b, and c, *see Appendix D*):
 - a. Has received three IV induction doses of an infliximab product prior to initiation;
 - b. Member is responding positively to an IV infliximab product;

- c. Member is unable to receive continued therapy with IV infliximab due to lack of caregiver or support system for assistance with administration and/or inadequate access to healthcare facility or home care interventions and/or lack of transportation to healthcare facility;
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 the following (a or b):
 - a. Avsola, Inflectra, Remicade/unbranded Remicade, Renflexis, IV: 5 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 5 mg/kg every 8 weeks.
 - b. Zymfentra, SC: 120 mg every 2 weeks starting at week 10.

Approval duration: 6 months**B. Ulcerative Colitis (must meet all):**

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 6 years;
4. Documentation of a Mayo Score ≥ 6 or modified Mayo Score ≥ 5 (*see Appendix F*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
6. Must meet one of the following (a or b):
 - a. Age ≥ 5 years: Failure of a ≥ 3 consecutive month trial of adalimumab (*Humira is preferred*)
 - b. Age ≥ 18 years: Failure of a ≥ 3 consecutive month trial of adalimumab Adalimumab-adbm and Simlandi[®] are) and tofacitinib (*Xeljanz/Xeljanz XR is preferred*), unless contraindicated or clinically significant adverse effects are experienced;
7. If request is for Zymfentra, provider attestation that member meets all of the following (a, b, and c, *see Appendix D*):
 - a. Has received three IV induction doses of an infliximab product prior to initiation;
 - b. Member is responding positively to an IV infliximab product;
 - c. Member is unable to receive continued therapy with IV infliximab due to lack of caregiver or support system for assistance with administration and/or inadequate access to healthcare facility or home care interventions and/or lack of transportation to healthcare facility;
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 5 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 5 mg/kg every 8 weeks.

Approval duration: 6 months

C. Rheumatoid Arthritis (must meet all):

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (*see Appendix H*);
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 MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
 - b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of at least ONE conventional disease-modifying antirheumatic drug [DMARD] (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel[®], Adalimumab-adbm, Simlandi[®], Cimzia, Xeljanz[®]/Xeljanz XR[®];
**Prior authorization is required for Enbrel, adalimumab products, Cimzia, 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 I*);
 - b. Routine assessment of patient index data 3 (RAPID3) score (*see Appendix J*);
7. Prescribed concomitantly with MTX, or another DMARD if intolerance or contraindication to MTX;
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 3 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 3 mg/kg every 8 weeks.

Approval duration: 6 months**D. Ankylosing Spondylitis** (must meet all):

1. Diagnosis of AS;
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 contraindicated or clinically significant adverse effects are experienced;
5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel[®], Adalimumab-adbm, Simlandi[®], Cimzia;

**Prior authorization is required for Enbrel, adalimumab products, and Cimzia*

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 5 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 5 mg/kg every 6 weeks.

Approval duration: 6 months

E. 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 at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel[®], Adalimumab-adbm, Simlandi[®], Cimzia[®], 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 5 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 5 mg/kg every 8 weeks.

Approval duration: 6 months

F. Plaque Psoriasis (must meet all):

1. Diagnosis of chronic-severe PsO as evidenced by involvement of one of the following (a or b):
 - a. $\geq 10\%$ of total body surface area;
 - b. Hands, feet, scalp, face, or genital area;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a, b, or c):
 - a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
 - b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of cyclosporine at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
 - c. Member has intolerance or contraindication to MTX and cyclosporine, and failure of phototherapy, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel[®], Adalimumab-adbm, Simlandi[®], Cimzia[®];

**Prior authorization is required for Enbrel, adalimumab products, Cimzia*

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 5 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 5 mg/kg every 8 weeks.

Approval duration: 6 months

G. Kawasaki Disease (off-label) (must meet all):

1. Diagnosis of Kawasaki disease;
2. Prescribed by or in consultation with a cardiologist, allergist, immunologist, infectious disease specialist, or rheumatologist;
3. Age ≥ 6 years;
4. Failure of immune globulin (Gammagard is preferred), unless contraindicated or clinically significant adverse effects are experienced;
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 a single infusion of 10 mg/kg given over 2 hours (see Appendix G for dose rounding guidelines).

Approval duration: 4 weeks (one time approval)

H. Other diagnoses/indications

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 2 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. Kawasaki Disease (off-label) (must meet all):

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

B. All Indications in Section I (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;

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- 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 meets one of the following (a or b):
 - a. For rheumatoid arthritis: member is responding positively to therapy as evidenced by one of the following (i or ii):
 - i. A decrease in CDAI (*see Appendix I*) or RAPID3 (*see Appendix J*) score from baseline;
 - ii. 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;
 - a. For all other indications: 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 regimen does not exceed one of the following (a, b, c, or d):
 - b. CD (i or ii):
 - i. 5 mg/kg every 8 weeks;
 - ii. 10 mg/kg every 8 weeks, if age ≥ 18 years and documentation supports inadequate response to current dose;
 - c. UC, PsA, PsO: 5 mg/kg every 8 weeks;
 - d. RA (i or ii):
 - i. 3 mg/kg every 8 weeks;
 - ii. If the request is for an increase in dose or dosing frequency (*dose and frequency should not be increased simultaneously*) from the current regimen, regimen does not exceed 10 mg/kg and/or every 4 weeks, and documentation supports both of the following (a and b):
 - a) Member has had an inadequate response to adherent use of Remicade/Inflectra/Renflexis concurrently with MTX or another DMARD;
 - b) One of the following (1 or 2):
 - 1) Current dosing frequency is every 8 weeks: member has received at least 4 doses (14 weeks of total therapy) of Avsola/Remicade/Inflectra/Renflexis;
 - 2) Current dosing frequency is $<$ every 8 weeks: member has received at least 2 doses of Avsola/Remicade/Inflectra/Renflexis at the current dosing frequency;
 - a. AS: 5 mg/kg every 6 weeks.

Approval duration: 12 months**C. 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 2 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 policies –CP.PMN.53 for Medicaid or evidence of coverage documents.

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, Simponi[®]], interleukin agents [e.g., Actemra[®] (IL-6RA) and its biosimilars, 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), Spevigo[®] (IL-36 antagonist), Stelara[®] (IL-12/23 inhibitor) and its biosimilars, Taltz[®] (IL-17A inhibitor), Tremfya[®] (IL-23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Cibinqo[™], Olumiant[™], Rinvoq[™], Xeljanz[®]/Xeljanz[®] XR,], anti-CD20 monoclonal antibodies [Rituxan[®] and its biosimilars], 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

6-MP: 6-mercaptopurine

AS: ankylosing spondylitis

CD: Crohn's disease

DMARD: disease-modifying antirheumatic drug

GI: gastrointestinal

MTX: methotrexate

NSAID: non-steroidal anti-inflammatory drug

PsA: psoriatic arthritis

PsO: psoriasis

RA: rheumatoid arthritis

TNF: tumor necrosis factor

UC: ulcerative colitis

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*, UC* 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
corticosteroids	CD* prednisone 40 mg PO QD for 2 weeks or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC [®]) 6-9 mg 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 [®])	PsO 2.5 mg/kg/day PO divided BID RA 2.5 – 4 mg/kg/day PO divided BID	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
leflunomide (Arava [®])	RA 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
6-mercaptopurine (Purixan [®])	CD*, UC* 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate (Rheumatrex [®])	CD*, UC* 15 – 25 mg/week IM or SC PsO 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	RA 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week	
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	AS Varies	Varies
Pentasa [®] (mesalamine)	CD, UC 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 2 g/day PO in divided doses UC <u>Initial dose:</u> <i>Adults:</i> 3 – 4 g/day PO in divided doses (not to exceed Q8 hrs) <i>6 years and older:</i> 40 – 60 mg/kg/day PO in 3 – 6 divided doses <u>Maintenance dose:</u> <i>Adults:</i> 2 g PO daily <i>6 years and older:</i> 30 mg/kg/day PO in 4 divided doses	RA: 3 g/day UC: 4 g/day
tacrolimus (Prograf [®])	CD* 0.27 mg/kg/day PO in divided doses or 0.15 – 0.29 mg/kg/day PO PsO 0.05 – 0.15 mg/kg/day PO	N/A
Cimzia [®] (certolizumab)	CD <u>Initial dose:</u> 400 mg SC at 0, 2, and 4 weeks <u>Maintenance dose:</u> 400 mg SC every 4 weeks PsA, RA, AS <u>Initial dose:</u> 400 mg SC at 0, 2, and 4 weeks	CD, PsA, RA, AS: 400 mg every 4 weeks PsO: 400 mg every other week

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<u>Maintenance dose:</u> 200 mg SC every other week (or 400 mg SC every 4 weeks) PsO 400 mg SC every other week. For some patients (with body weight ≤ 90 kg), a dose of 400 mg SC at 0, 2 and 4 weeks, followed by 200 mg SC every other week may be considered.	
Xeljanz [®] (tofacitinib)	PsA, UC, RA 5 mg PO BID	10 mg/day
Xeljanz XR [®] (tofacitinib extended-release)	PsA, UC, RA 11 mg PO QD	11 mg/day
Humira [®] (adalimumab)	CD <u>Initial dose:</u> <i>Adults:</i> 160 mg SC on Day 1, then 80 mg SC on Day 15 <i>Pediatrics:</i> Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 80 mg SC on Day 1, then 40 mg SC on Day 15 Weight ≥ 40 kg (88 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15 <u>Maintenance dose:</u> <i>Adults:</i> 40 mg SC every other week starting on Day 29 <i>Pediatrics:</i> Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 20 mg SC every other week starting on Day 29 Weight ≥ 40 kg (88 lbs): 40 mg SC every other week starting on Day 29 UC <u>Initial dose:</u>	40 mg every other week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	160 mg SC on Day 1, then 80 mg SC on Day 15 <u>Maintenance dose:</u> 40 mg SC every other week starting on Day 29 PsA, AS 40 mg SC every other week PsO <u>Initial dose:</u> 80 mg SC <u>Maintenance dose:</u> 40 mg SC every other week starting one week after initial dose RA 40 mg SC every other week Some patients with RA not receiving concomitant methotrexate may benefit from increasing the frequency to 40 mg every week.	
Enbrel® (etanercept)	AS 50 mg SC once weekly PsA, RA 25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week

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):
 - Doses > 5 mg/kg in patients with moderate-to-severe heart failure
 - Re-administration to patients who have experienced a severe hypersensitivity reaction to infliximab products
 - Known hypersensitivity to inactive components of the product or to any murine proteins

- Boxed warning(s):
 - Serious infections
 - Malignancy

Appendix D: General Information

- Contraindications:
- Definition of failure of MTX or DMARDs
 - 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
- Infliximab used in the treatment of unspecified iridocyclitis (anterior uveitis) has primarily been evaluated in case reports and uncontrolled case series. One phase II clinical trial by Suhler and associates (2009) reported the 2-year follow-up data of patients with refractory uveitis treated with intravenous infliximab as part of a prospective clinical trial. Their 1-year data, published in 2005 (Suhler, 2005) reported reasonable initial success, but an unexpectedly high incidence of adverse events. Of their 23 patients, 7 developed serious adverse events, including 3 thromboses, 1 malignancy, 1 new onset of congestive heart failure, and 2 cases of drug-induced lupus. The American Optometric Association anterior uveitis clinical practice guidelines recommend alternative therapies that include ophthalmic corticosteroids (e.g., prednisolone, dexamethasone, fluoromethalone) and anticholinergics (e.g., atropine, cyclopentolate, homatropine). If the disease has not responded to topical therapy, oral corticosteroids can be considered.
- Zymfentra is indicated as maintenance treatment only, starting at week 10 and thereafter. All patients must complete an intravenous induction regimen with an infliximab product before starting Zymfentra. To switch patients who are responding to maintenance therapy with an infliximab product administered intravenously, administer the first subcutaneous dose of Zymfentra in place of the next scheduled intravenous infusion and every two weeks thereafter.

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:

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- 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, stricturing or stenosis disease and/or phenotype
 - Intestinal obstruction or abscess
- High risk factors for postoperative recurrence may include:
 - Less than 10 years duration between time of diagnosis and surgery
 - Disease location in the ileum and colon
 - Perianal fistula
 - Prior history of surgical resection
 - Use of corticosteroids prior to surgery

Appendix F: Mayo Score or Modified 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

- Modified Mayo Score: developed from the full Mayo score and evaluates ulcerative colitis stage, based on three parameters: stool frequency, rectal bleeding, and endoscopic evaluation. The modified Mayo Score gives a maximum overall score of 9. The FDA currently accepts the modified Mayo Score for the assessment of disease activity in pivotal UC clinical trials.

Appendix G: Dose Rounding Guidelines

Weight-based Dose Range	Vial Quantity Recommendation
≤ 104.99 mg	1 vial of 100 mg/20 mL
105 to 209.99 mg	2 vials of 100 mg/20 mL
210 to 314.99 mg	3 vials of 100 mg/20 mL
325 to 419.99 mg	4 vials of 100 mg/20 mL
420 to 524.99 mg	5 vials of 100 mg/20 mL
525 to 629.99 mg	6 vials of 100 mg/20 mL
630 to 734.99 mg	7 vials of 100 mg/20 mL
735 to 839.99 mg	8 vials of 100 mg/20 mL

Appendix H: 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
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 I: 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 J: 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

RAPID3 Score	Disease state interpretation
3.1 to 6	Low disease activity
6.1 to 12	Moderate disease activity
> 12	High disease activity

I. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CD, UC	<u>Initial dose:</u> <i>Adults/Pediatrics:</i> 5 mg/kg IV at weeks 0, 2 and 6 <u>Maintenance dose:</u> <i>Adults/Pediatrics:</i> 5 mg/kg IV every 8 weeks. For CD: Some adult patients who initially respond to treatment may benefit from increasing the dose to 10 mg/kg if they later lose their response	CD, Adults: 10 mg/kg every 8 weeks UC, Adults: 5 mg/kg every 8 weeks Pediatrics: 5 mg/kg every 8 weeks
PsA	<u>Initial dose:</u> 5 mg/kg IV at weeks 0, 2 and 6 <u>Maintenance dose:</u> 5 mg/kg IV every 8 weeks	5 mg/kg every 8 weeks
PsO		
RA	In conjunction with MTX <u>Initial dose:</u> 3 mg/kg IV at weeks 0, 2 and 6 <u>Maintenance dose:</u> 3 mg/kg IV every 8 weeks Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks	10 mg/kg every 4 weeks
AS	<u>Initial dose:</u> 5 mg/kg IV at weeks 0, 2 and 6 <u>Maintenance dose:</u> 5 mg/kg IV every 6 weeks	5 mg/kg every 6 weeks

II. Product Availability

Drug Name	Availability
Infliximab (Remicade)	Single-use vial: 100 mg/20 mL
Infliximab-axxq (Avsola)	Single-dose vial: 100 mg/20 mL
Infliximab-dyyb (Inflectra)	Single-use vial: 100 mg/20 mL
Infliximab-abda (Renflexis)	Single-use vial: 100 mg/20 mL

III. References

1. Remicade Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; October 2021. Available at: <https://www.remicade.com/>. Accessed February 8, 2025.
2. Avsola Prescribing Information. Thousand Oaks, CA: Amgen Inc.; September 2021. Available at: <https://www.avsola.com/>. Accessed February 8, 2023.
3. Inflectra Prescribing Information. Lake Forest, IL: Hospira, a Pfizer Company; September 2021. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=9271>. Accessed February 8, 2023.
4. Renflexis Prescribing Information. Kenilworth, NJ: Merck & Co; January 2023. Available at: <https://www.renflexis.com/>. Accessed February 8, 2023.
5. Zymfentra Prescribing Information. Incheon, Republic of Korea: Celltrion, Inc; February 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761358Orig1s001lbl.pdf. Accessed February 27, 2025.
6. Bernell O, Lapidus A, Hellers G. Risk Factors for Surgery and Postoperative Recurrence in Crohn's Disease. *Annals of Surgery*. 2000; 231(1): 38-45.
7. American Optometric Association Clinical Practice Guideline: Care of the Patient with Anterior Uveitis. Reviewed 2004. Available at: <https://www.aoa.org/documents/optometrists/CPG-7.pdf>.
8. Suhler EB, Smith JR, Wertheim MS, et al. A prospective trial of infliximab therapy for refractory uveitis: Preliminary safety and efficacy outcomes. *Arch Ophthalmol*. 2005;123(7):903-912.
9. Menter A, Gottlieb A, Feldman SR, et al. Guidelines for the management of psoriasis and psoriatic arthritis. Section 1: Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2008;58(5):826-850.
10. Suhler EB, Smith JR, Giles TR, et al. Infliximab therapy for refractory uveitis: 2-year results of a prospective trial. *Arch Ophthalmol*. 2009;127(6):819-822.
11. Braun J, van den berg R, et al. 2010 Update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Am Rheum Dis*. 2011; 70; 896-904.
12. McCrindle B, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease. *Circulation*. 2017;135:e927-e999.
13. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
14. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Ann Rheum Dis*. 2014; 73: 492-509.
15. Sandborn WJ. Crohn's Disease Evaluation and Treatment: Clinical Decision Tool. *Gastroenterol* 2014; 147: 702-705.
16. 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

17. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guidelines for the Treatment of Rheumatoid Arthritis. *Arthritis Care & Research*. 2015; 68(1):1-26.
18. Ward MM, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis & Rheumatology*, 2015. DOI 10.1002/ART.39298.
19. Lichtenstein GR, Loftus Jr. EV, Isaacs KI, Regueiro MD, Gerson LB, and Sands BE. ACG clinical guideline: management of Crohn's disease in adults. *Am J Gastroenterol*. 2018; 113:481-517.
20. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80:1029-72. doi:10.1016/j.aad.201811.057.
21. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Am J Gastroenterol*. 2019;114:384-413.
22. Fraenkel L, Bathon JM, Enggland BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care & Research*. 2021; 73(7):924-939. DOI 10.1002/acr.24596.
23. Ulcerative Colitis: Clinical Trial Endpoints Guidance for Industry. Silver Spring, MD. Food and Drug Administration.; July 2016. Available at: <https://www.fda.gov/files/drugs/published/Ulcerative-Colitis--Clinical-Trial-Endpoints-Guidance-for-Industry.pdf>. Accessed February 3, 2025.
24. Naegeli AN, Hunter T, Dong Y, et al. Full, Partial, and Modified Permutations of the Mayo Score: Characterizing Clinical and Patient-Reported Outcomes in Ulcerative Colitis Patients. *Crohn's Colitis* 360. 2021 Feb 23;3(1):otab007. doi: 10.1093/crocol/otab007. PMID: 36777063; PMCID: PMC9802037.
25. Singh S, Loftus EV Jr, Limketkai BN, et al. AGA Living Clinical Practice Guideline on Pharmacological Management of Moderate-to-Severe Ulcerative Colitis. *Gastroenterology*. 2024 Dec;167(7):1307-1343. doi: 10.1053/j.gastro.2024.10.001. PMID: 39572132.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1745	Injection, infliximab, excludes biosimilar, 10 mg
Q5103	Injection, infliximab-dyyb, biosimilar, (inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (renflexis), 10 mg
J1748	Injection, infliximab-dyyb (zymfentra), 10 mg
Q5121	Injection, infliximab-axxq, biosimilar, (avsola), 10 mg

CLINICAL POLICY

Infliximab, Infliximab-dyyb, Infliximab-abda



HCPCS Codes	Description
S9359	Home infusion therapy, anti-tumor necrosis factor intravenous therapy; (e.g., Infliximab); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created, adapted IL.PHAR.254 to align with HFS criteria	1.22.24	
2Q 2025 Annual Review: updated preferred adalimumab products;for CD and UC, added additional requirement for Zymfentra requests requiring provider attestation that “member is unable to receive continued therapy with IV infliximab due to lack of caregiver or support system for assistance with administration and/or inadequate access to healthcare facility or home care interventions and/or lack of transportation to healthcare facility.” for UC initial criteria, added option for documentation of modified Mayo Score ≥ 5 ; for Appendix F, added supplemental information on modified Mayo Score; for Kawasaki disease, updated maximum dose from 5 mg/kg given over 2 hours to 10 mg/kg given over 2 hours; for continued therapy section, removed “if new dosing regimen, approve for 6 months” for approval duration; updated section III.B with Spevigo and biosimilar verbiage; references reviewed and updated.	4.17.25	
Removed references to adalimumab-ryvk	7.31.25	

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.

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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.

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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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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