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

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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®) and infliximab-abda (Renflexis™), are tumor necrosis factor (TNF) blockers.

FDA Approved Indication(s)

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):
  - 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.

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, 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 (*Humira is preferred*)
   b. Age ≥ 18 years: Failure of a ≥ 3 consecutive month trial of adalimumab (*Humira is preferred*) and certolizumab (*Cimzia is preferred*), unless contraindicated or clinically significant adverse effects are experienced;
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. 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

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 (*see Appendix F*)
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
6. Must meets 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 (*Humira is preferred*) and tofacitinib (*Xeljanz/Xeljanz XR is preferred*), unless contraindicated or clinically significant adverse effects are experienced;
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

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®, Humira®, Cimzia, Xeljanz®/Xeljanz XR®;
   **Prior authorization is required for Enbrel, Humira, 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®, Humira®, Cimzia;
   **Prior authorization is required for Enbrel, Humira, 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®, Humira®, Cimzia®, Xeljanz®/Xeljanz XRMember 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. 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. ≥ 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®, Humira®, Cimzia®;
   **Prior authorization is required for Enbrel, Humira, 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 5 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. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
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. If request is for a dose increase, new regimen does not exceed one of the following (a, b, c, or d):
   a. 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;
   b. UC, PsA, PsO: 5 mg/kg every 8 weeks;
   c. 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 *(If new dosing regimen, approve for 6 months)*

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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.

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®, 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® (IL12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL17RA), 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

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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** 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 **RA** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/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** Initial dose: *Adults:* 3 – 4 g/day PO in divided doses (not to exceed Q8 hrs) *6 years and older:* 40 – 60 mg/kg/day PO in 3 – 6 divided doses Maintenance dose: *Adults:* 2 g PO daily	RA: 3 g/day UC: 4 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	6 years and older: 30 mg/kg/day PO in 4 divided doses	
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** Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 400 mg SC every 4 weeks **PsA, RA, AS** 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) **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.	CD, PsA, RA, AS: 400 mg every 4 weeks PsO: 400 mg every other week
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** Initial dose: *Adults:* 160 mg SC on Day 1, then 80 mg SC on Day 15 *Pediatrics:* Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 80 mg SC on Day 1, then 40 mg SC on Day 15	40 mg every other week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Weight ≥ 40 kg (88 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: *Adults:* 40 mg SC every other week starting on Day 29 *Pediatrics:* 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** 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 **PsA, AS** 40 mg SC every other week **PsO** Initial dose: 80 mg SC Maintenance dose: 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	50 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	PsA, RA 25 mg SC twice weekly or 50 mg SC once weekly	

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.

Appendix E: Immunomodulator 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, 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

- 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

- The following may be considered for medical justification supporting inability to use an immunomodulator for ulcerative colitis:
  - Documentation of Mayo Score 6 – 12 indicative of moderate to severe ulcerative colitis.

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 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 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
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	Initial dose: *Adults/Pediatrics:* 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: *Adults/Pediatrics:* 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 PsO	Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 8 weeks	5 mg/kg every 8 weeks
RA	In conjunction with MTX Initial dose: 3 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 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	Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 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

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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
Q5102	Injection, infliximab, biosimilar, 10 mg
Q5103	Injection, infliximab-dyyb, biosimilar, (inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (renflexis), 10 mg
Q5121	Injection, infliximab-axxq, biosimilar, (avsola), 10 mg
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 CP.PHAR.254 Infliximab (Remicade Renflexis Inflectra) policy.	12.9.19	1.7.20
4Q 2020 annual review added Avsola and reviewed references	12.20.20	
Changes:	4.20.21	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added requirement for Mayo score of at least 6 and Age ≥ 5 years: Failure of a ≥ 3 consecutive month trial of adalimumab (*Humira is preferred*) for UC; added dose rounding guidelines for all indications; added requirement for redirection to Inflectra and Renflexis to Section II for Remicade continued therapy requests; 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. Added criteria for RAPID3 assessment for RA given limited in-person visits during COVID-19 pandemic, updated appendices.		
Changes for UC, revised redirection from AZA, 6-MP, ASA to systemic corticosteroids and removed trial of Added HCPCS code for Avsola	9.2.21	
3Q2022 annual review: for PsO, allowed phototherapy as alternative to systemic conventional DMARD if contraindicated or clinically significant adverse effects are experienced; added off-label use for Kawasaki disease; removed unspecified iridocyclitis (ICD10 H20.9) from Section III; revised redirection language to biosimilars to "must use" to clarify intent; reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated; references reviewed and updated	9.8.22	

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.

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.