Clinical Policy: Infliximab (Remicade), Infliximab-axxq (Avsola), Infliximab-dyyb (Inflectra), and Infliximab-abda (Renflexis)

Reference Number: CP.PHAR.254
Effective Date: 07.16
Last Review Date: 02.21
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. 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. If request is for Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
6. Dose does not exceed 5 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 5 mg/kg every 6 weeks (*see Appendix G for dose rounding guidelines*).

Approval duration: 6 months

B. Crohn's Disease (must meet all)**:**
1. Diagnosis of CD;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 6 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], 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 E*);
5. If request is for Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
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 (*see Appendix G for dose rounding guidelines*).

Approval duration: 6 months

C. Plaque Psoriasis (must meet all)**:**
1. Diagnosis of PsO;
2. Prescribed by or in consultation with a dermatologist or 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 effects are experienced;
b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

5. If request is for Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
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 (*see Appendix G for dose rounding guidelines*).

Approval duration: 6 months

D. 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. If request is for Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
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 (*see Appendix G for dose rounding guidelines*).

Approval duration: 6 months

E. 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. 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)*;
6. Prescribed concomitantly with MTX, or another DMARD if intolerance or contraindication to MTX;
7. If request is for Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
8. Dose does not exceed 3 mg/kg at weeks 0, 2, and 6, followed by maintenance dose of 3 mg/kg every 8 weeks (*see Appendix G for dose rounding guidelines*).

Approval duration: 6 months

F. 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. If request is for Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
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 (*see Appendix G for dose rounding guidelines*).

Approval duration: 6 months

G. 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. 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 Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
4. If request is for a dose increase, new regimen does not exceed one of the following (*see Appendix G for dose rounding guidelines*) (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)*

B. 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. Unspecified iridocyclitis (ICD10 H20.9).

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
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO QD	50 mg/day
azathioprine (Azasan®, Imuran®)	**RA** 1 mg/kg/day PO QD or divided BID **CD*** 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*** Initial dose: 125 or 250 mg PO QD Maintenance dose: 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*** 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*** 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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	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

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:
  - Remicade/Avsola/Renflexis/Inflectra doses > 5 m/kg should not be administered to patients with moderate to severe heart failure. Remicade doses of 10 mg/kg were shown to be associated with an increased incidence of death and hospitalization due to worsening heart failure in clinical trials.
- 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

V. 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:	10 mg/kg every 4 weeks

Indication	Dosing Regimen	Maximum 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	
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

VI. 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

VII. References

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treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis & Rheumatology*, 2015. DOI 10.1002/ART.39298.
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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
Q5103	Injection, infliximab-dyyb, biosimilar, (inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (renflexis), 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
Humira preferencing in pediatric Crohn's is removed.	03.17	
Converted to new template. Removed limitations based on labeled warnings and precautions. RA: modified the RA diagnostic criteria from requiring one or more of the following: ≥ 5 inflamed joints, elevated ESR and/or CRP; positive rheumatoid factor and/or anticyclic citrullinated peptide (CCP) antibodies; evidence of inflammation on plain radiography of the hands, wrists, or feet, such as osteopenia and/or periarticular swelling, to the ACR diagnostic criteria. PsA: changed option of contraindication to hydroxychloroquine to cyclosporine. PsO: removed redirection to Enbrel and Humira. AS: added prescriber restriction. CD: updated list of poor prognostic indicators. UC: change required trials form immunomodulator to specifically thiopurines and removed MTX as example of acceptable trial; removed redirection to Humira. Added Renflexis.	07.17	07.17
2Q 2018 annual review: removed TB testing requirement from all criteria; removed requirements for specific criteria relating to diagnosis for CD and PsO; modified gastroenterologist specialty requirement to gastrointestinal specialist for CD/UC; modified preferencing for infliximab products for all indications, added aminosalicylate as an option for trial and failure for UC; modified trial and failure for RA to at least one conventional DMARD; added requirement for concomitant use of MTX or another DMARD for RA; removed trial and failure of phototherapy and topical therapy for PsO; modified trial and failure for PsO to require methotrexate (or another agent if methotrexate is not tolerated or contraindicated); added specific max dosing requirements for continued therapy approval; references reviewed and updated.	02.27.18	05.18
4Q 2018 annual review: added HIM; modified prescriber specialist from GI specialist to gastroenterologist for CD and UC; added trial and failure of immunosuppressants, or medical necessity for use of biologics in CD; allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.	09.04.18	11.18
Removed redirections to Humira and/or Enbrel for all indications per SDC decision in line with previously approved clinical guidance.	12.21.18	
2Q 2019 annual review: removed trial and failure requirement of conventional DMARDs (e.g., MTX)/NSAIDs for biologic DMARDs for PsA per ACR/NPF 2018 guidelines; references reviewed and updated.	03.05.19	05.19
RT4: updated FDA-approved language to indicate Inflectra and Renflexis are approved for use in pediatric ulcerative colitis; removed age ≥ 18 requirement in Remicade redirection.	07.09.19	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added unspecified iridocyclitis to Section III as an excluded use for Inflectra, Remicade, and Renflexis. Updated coding implications table with biosimilar HCPCS codes. Removed HIM line of business.	01.14.19	02.20 (ad hoc)
2Q 2020 annual review: added AVsola to the policy; for UC, revised redirection from AZA, 6-MP, ASA to systemic corticosteroids, and added requirement for Mayo score of at least 6; 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.	04.23.20	05.20
Per November SDC and prior clinical guidance, added redirection to Inflectra and Renflexis for Avsola; ad hoc: revised typo in Appendix E from "normal ESR" to "abnormal ESR" for a point gained for ACR Classification Criteria.	11.16.20	
Added criteria for RAPID3 assessment for RA given limited in-person visits during COVID-19 pandemic, updated appendices.	11.24.20	02.21

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.