

Clinical Policy: Infliximab (Remicade) and Infliximab-dyyb (Inflectra)

Reference Number: CP.PHAR.254

Effective Date: 07/16

Last Review Date: 12/16

[Coding Implications](#)
[Revision Log](#)

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

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene[®] clinical policy for infliximab (Remicade[®]) and infliximab-dyyb (Inflectra):

Policy/Criteria

It is the policy of health plans affiliated with Centene Corporation[®] that Remicade and Inflectra are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Crohn's Disease (must meet all):

1. Prescribed by or in consultation with a gastroenterologist;
2. Age \geq 6 years;
3. If request is for Remicade, member has a contraindication or intolerance to Inflectra;
4. Diagnosis of moderately to severely active Crohn's disease (CD) and (a or b):
 - a. Has one of the following poor prognostic indicators for CD:
 - i. Age < 18 years;
 - ii. Perianal disease;
 - iii. Upper gastrointestinal tract involvement;
 - iv. Multiple extra-intestinal manifestations;
 - v. Active tobacco use;
 - vi. Perforating (i.e., fistulizing) disease;
 - b. Member has failed one of the following therapies unless intolerant or contraindicated:
 - i. A biologic for CD other than Remicade/Inflectra;
 - ii. An immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], methotrexate [MTX]) for \geq 3 consecutive months;
5. Member has failed Humira for \geq 3 consecutive months unless intolerant or contraindicated;
6. Tuberculosis (TB) test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
7. After initial dosage regimen, prescribed maintenance dosing of Remicade/Inflectra is not more frequent than every 8 weeks;
8. Member has none of the following contraindications:
 - a. Known hypersensitivity to Remicade/Inflectra or any of their components;
 - b. Active, serious infection;
 - c. Moderate to severe heart failure (if requesting Remicade doses > 5 mg/kg);
 - d. Symptoms or signs of liver dysfunction (e.g., jaundice, liver enzyme elevations \geq 5 times the upper limit of normal).

Approval duration: 6 months

B. Ulcerative Colitis (must meet all):

1. Prescribed by or in consultation with a gastroenterologist;
2. Age \geq 6 years;
3. If age is \geq 18 years and request is for Remicade, member has a contraindication or intolerance to Inflectra;
4. Diagnosis of moderately to severely active ulcerative colitis (UC);
5. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
6. Member has failed one of the following therapies for \geq 3 months unless intolerant or contraindicated:
 - a. A biologic for UC other than Remicade/Inflectra;
 - b. An immunomodulator (e.g., azathioprine, 6MP, MTX) for \geq 3 consecutive months;
7. Member has failed Humira for \geq 3 consecutive months unless intolerant or contraindicated;
8. After initial dosage regimen, prescribed maintenance dosing of Remicade/Inflectra is not more frequent than every 8 weeks;
9. Member has none of the following contraindications:
 - a. Known hypersensitivity to Remicade/Inflectra or any of their components;
 - b. Active, serious infection;
 - c. Moderate to severe heart failure (if requesting Remicade doses $>$ 5 mg/kg)
 - d. Symptoms or signs of liver dysfunction (e.g., jaundice, liver enzyme elevations \geq 5 times the upper limit of normal).

Approval duration: 6 months

C. Rheumatoid Arthritis (must meet all):

1. Prescribed by or in consultation with a rheumatologist;
2. Age \geq 18 years;
3. If request is for Remicade, member has a contraindication or intolerance to Inflectra;
4. Diagnosis of rheumatoid arthritis (RA) and one or more of the following indications of moderate to severe disease:
 - a. \geq 5 inflamed joints;
 - b. Elevation in the erythrocyte sedimentation rate (ESR) and/or serum C-reactive protein (CRP) concentration;
 - c. Positive rheumatoid factor and/or anticyclic citrullinated peptide (CCP) antibodies (present in most patients);
 - d. Evidence of inflammation on plain radiography of the hands, wrists, or feet, such as osteopenia and/or periarticular swelling;
5. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the patient has received treatment for latent TB infection;
6. Member has failed one of the following therapies unless intolerant or contraindicated:
 - a. A biologic for RA other than Remicade/Inflectra;

- b. MTX for ≥ 3 consecutive months;
- c. If intolerance or contraindication to MTX, sulfasalazine, leflunomide, or hydroxychloroquine for ≥ 3 consecutive months;
- 7. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
- 8. Prescribed concomitantly with MTX, or another disease-modifying antirheumatic (DMARD) agent if intolerance or contraindication to MTX;
- 9. After initial dosage regimen, prescribed maintenance dosing of Remicade/Inflectra is not more frequent than every 4 weeks;
- 10. Member has none of the following contraindications:
 - a. Known hypersensitivity to Remicade/Inflectra or any of their components;
 - b. Active, serious infection;
 - c. Moderate to severe heart failure (if requesting Remicade doses > 5 mg/kg);
 - d. Symptoms or signs of liver dysfunction (e.g., jaundice, liver enzyme elevations ≥ 5 times the upper limit of normal).

Approval duration: 6 months

D. Ankylosing Spondylitis (must meet all):

- 1. Age ≥ 18 years;
- 2. If request is for Remicade, member has a contraindication or intolerance to Inflectra;
- 3. Diagnosis of active ankylosing spondylitis (AS);
- 4. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
- 5. Member has failed one of the following therapies unless intolerant or contraindicated:
 - a. A biologic for AS other than Remicade/Inflectra;
 - b. Two or more non-steroidal anti-inflammatory drugs (NSAIDs) at maximum tolerated doses, each for ≥ 4 weeks;
- 6. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
- 7. After initial dosage regimen, prescribed maintenance dosing of Remicade/Inflectra is not more frequent than every 6 weeks;
- 8. Member has none of the following contraindications:
 - a. Known hypersensitivity to Remicade/Inflectra or any of their components;
 - b. Active, serious infection;
 - c. Moderate to severe heart failure (if requesting Remicade doses > 5 mg/kg);
 - d. Symptoms or signs of liver dysfunction (e.g., jaundice, liver enzyme elevations ≥ 5 times the upper limit of normal).

Approval duration: 6 months

E. Psoriatic Arthritis (must meet all):

- 1. Prescribed by or in consultation with a dermatologist or rheumatologist;
- 2. Age ≥ 18 years;
- 3. If request is for Remicade, member has a contraindication or intolerance to Inflectra;
- 4. Diagnosis of active psoriatic arthritis (PsA);

5. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
6. Member has failed one of the following therapies unless intolerant or contraindicated:
 - a. A biologic for PsA other than Remicade/Inflectra;
 - b. MTX for ≥ 3 consecutive months;
 - c. If intolerance or contraindication to MTX, sulfasalazine, leflunomide, cyclosporine, or azathioprine, for ≥ 3 consecutive months;
7. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
8. After initial dosage regimen, prescribed maintenance dosing of Remicade/Inflectra is not more frequent than every 8 weeks;
9. Member has none of the following contraindications:
 - a. Known hypersensitivity to Remicade/Inflectra or any of their components;
 - b. Active, serious infection;
 - c. Moderate to severe heart failure (if requesting Remicade doses > 5 mg/kg);
 - d. Symptoms or signs of liver dysfunction (e.g., jaundice, liver enzyme elevations ≥ 5 times the upper limit of normal).

Approval duration: 6 months

F. Plaque Psoriasis (must meet all):

1. Prescribed by or in consultation with a dermatologist or rheumatologist;
2. Age ≥ 18 years;
3. If request is for Remicade, member has a contraindication or intolerance to Inflectra;
4. Diagnosis of chronic severe (i.e., extensive and/or disabling) plaque psoriasis (PsO) and one or more of the following (a or b):
 - a. Greater than 5% of body surface area is affected;
 - b. Involvement of palms, soles, face/neck, body folds, or genitalia;
5. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
6. Member has failed phototherapy and a topical therapy (e.g., calcipotriene, coal tar preparations, medium-to-high potency corticosteroids, anthralin, tazarotene);
7. Member has failed one of the following therapies unless intolerant or contraindicated:
 - a. A biologic for PsO other than Remicade/Inflectra;
 - b. One or more systemic therapies (e.g., MTX, cyclosporine, acitretin, thioguanine) for ≥ 3 consecutive months;
8. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
9. After initial dosage regimen, prescribed maintenance dosing of Remicade/Inflectra is not more frequent than every 8 weeks;
10. Member has none of the following contraindications:
 - a. Known hypersensitivity to Remicade/Inflectra or any of their components;
 - b. Active, serious infection;
 - c. Moderate to severe heart failure (if requesting Remicade doses > 5 mg/kg);
 - d. Symptoms or signs of liver dysfunction (e.g., jaundice, liver enzyme elevations ≥ 5 times the upper limit of normal).

Approval duration: 6 months

G. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. All Indications (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member responding positively to therapy;
3. Prescribed maintenance dosing of Remicade/Inflectra is not more frequent than the following:
 - a. AS: dosing frequency of every 6 weeks;
 - b. RA: dosing frequency of every 4 weeks;
 - c. All other indications: dosing frequency of every 8 weeks;
4. Member has none of the following reasons to discontinue:
 - a. Known hypersensitivity to Remicade/Inflectra or any of their components;
 - b. Active, serious infection;
 - c. Moderate to severe heart failure (if requesting Remicade doses > 5 mg/kg);
 - d. Symptoms or signs of liver dysfunction (e.g., jaundice, liver enzyme elevations ≥ 5 times the upper limit of normal).

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Infliximab is a chimeric monoclonal antibody that binds to human tumor necrosis factor alpha (TNF α), thereby interfering with endogenous TNF α activity. Elevated TNF α levels have been found in involved tissues/fluids of patients with RA, AS, PsA, PsO, CD and UC. Biological activities of TNF α include the induction of proinflammatory cytokines (interleukins), enhancement of leukocyte migration, activation of neutrophils and eosinophils, and the induction of acute phase reactants and tissue degrading enzymes. Animal models have shown TNF α expression causes polyarthritis, and infliximab can prevent disease as well as allow diseased joints to heal.

Formulations:

Solution Reconstituted, Intravenous [preservative free]:

Remicade (infliximab): 100 mg (1 ea) [contains polysorbate 80]

Inflectra (infliximab-dyyb): 100 mg (contains polysorbate 80, sucrose 500 mg; biosimilar agent)

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FDA Approved Indications:

Remicade and Inflectra* are tumor necrosis factor-alpha inhibitors/intravenous injectable formulations indicated for:

- Crohn’s Disease: 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. Remicade is indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD.
- Pediatric Crohn’s Disease: 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: 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 Ulcerative Colitis: 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 in combination with methotrexate: Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active RA.
- Ankylosing Spondylitis: Reducing signs and symptoms in patients with active AS.
- Psoriatic Arthritis: Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with PsA.
- Plaque Psoriasis: 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.

**Inflectra is FDA approved for all indications above except pediatric UC.*

Appendices

Appendix A: Abbreviation Key

AS: ankylosing spondylitis	PsA: psoriatic arthritis
CCP: citrullinated peptide	PsO: psoriasis
CD: Crohn’s disease	RA: rheumatoid arthritis
CRP: C-reactive protein	SC: subcutaneous
DMARD: disease modifying antirheumatic drug	TB: tuberculosis
ESR: erythrocyte sedimentation rate	TNF: tumor necrosis factor
MTX: methotrexate	UC: ulcerative colitis

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-

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date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1745	Injection infliximab, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date
<p>Policy split from CP.PHAR.86.ArthritisTreatments, CP.PHAR.85.Psoriasis Treatments, CP.PHAR.87.IBD Treatment_4_</p> <p>Added the biosimilar Inflectra (approved for all Remicade indications with the exception of pediatric UC).</p> <p>CD, UC, RA, PsA, AS, PsO: Removed criteria related to HBV, malignant disease, concomitant use with other biologics, and concurrent administration of live vaccines; added dosing.</p> <p>CD: modified criteria requiring failure of immunomodulator, corticosteroids or aminosalicilate to failure of “corticosteroid, with or without immunomodulator” per 2014 AGA Clinical decision tool.</p> <p>RA: changed age requirement to 18; modified criteria to require trial of MTX, unless contraindicated; added sulfasalazine and hydroxychloroquine as an alternative to MTX if contraindicated; Required trial of Humira AND Enbrel instead of one or the other. Added option for other DMARD if concomitant admin of MTX contraindicated.</p> <p>AS: added option of trial of a different biologic in addition to NSAIDs. Required trial of Humira AND Enbrel instead of one or the other.</p> <p>PsA: Added requirements for failure of a different biologic or 2 or more DMARDs, not including Otezla.</p> <p>PsO: removed duration of trial for topical and phototherapy; Added option for trial of a different biologic. Required trial of Humira and Enbrel, instead of previous requirement of Humira or Enbrel.</p> <p>Re-auth: combined into All Indications; added criteria for dosing and reasons to discontinue; for PsO changed efficacy criteria related to Psoriasis Area and Severity Index (PASI)-75 to general efficacy statement.</p> <p>Modified approval duration to 6 months for initial and 12 months for renewal.</p>	07/16	07/16
<p>Added preferencing for Inflectra prior to allowing Remicade, except for UC patients aged 6-18.</p> <p>CD: Removed corticosteroid as an option for trial/failure.</p> <p>UC: removed aminosalicylates and corticosteroids as potential acceptable first-line therapies.</p> <p>PsA: Preferenced trial of MTX above other DMARDs.</p> <p>Specialist review by dermatologist, rheumatologist, and gastroenterologist.</p>	11/16	12/16

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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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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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