Infliximab

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the infliximab drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies for Remicade (infliximab), Inflectra (infliximab-dyyb), Renflexis (infliximab-abda), and Avsola (infliximab-axxq). For this program, Avsola, Inflectra, Renflexis, Entyvio, Stelara, and Simponi Aria are the preferred products. Coverage for non-preferred products is provided based on clinical circumstances that would exclude the use of the preferred product(s) and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. Submission of medical records documenting relevant history, physician evaluation information, and supporting compendia or current literature (if applicable) will be required for review of these exceptions.

FDA-Approved Indications

1. Moderately to severely active Crohn’s disease (CD)
2. Moderately to severely active ulcerative colitis (UC)
3. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
4. Active ankylosing spondylitis (AS)
5. Active psoriatic arthritis (PsA)
6. Chronic severe plaque psoriasis (PsO)

Compendial Uses

1. Axial spondyloarthritis
2. Behçet’s syndrome
3. Granulomatosis with polyangiitis (Wegener’s granulomatosis)
4. Hidradenitis suppurativa
5. Juvenile idiopathic arthritis

6. Pyoderma gangrenosum
7. Sarcoidosis
8. Takayasu's arteritis
9. Uveitis
10. Reactive arthritis
11. Immune checkpoint inhibitor toxicity

POLICY

Must meet BOTH the Preferred Drug Plan Design and Criteria for Initial Approval/Continuation of Therapy when both are applicable.

Preferred Drug Plan Design

Coverage for a non-preferred product is provided when both of the following criteria are met:

- Member has a documented intolerable adverse event with all of the preferred products, Avsola, Inflectra, and Renflexis, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.
- Member has a documented inadequate response or intolerable adverse event with Entyvio, Ilumya, and Simponi Aria where the product's indications overlap.

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

	Products	
Preferred	• **Avsola** (infliximab-axxq) • **Entyvio** (vedolizumab) • **Inflectra** (infliximab-dyyb) • **Renflexis** (infliximab-abda)	• **Simponi Aria** (golimumab, intravenous) • **Stelara IV** (ustekinumab)*
Targeted	• **Actemra** (tocilizumab) • **Orencia** (abatacept)	• **Remicade** (infliximab)

*Stelara IV is indicated for a one time induction dose for Crohn's disease and ulcerative colitis.

Criteria for Initial Approval

A) Moderately to severely active Crohn's disease (CD)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of moderately to severely active Crohn's disease.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active Crohn's disease in members who had an inadequate response, intolerance, or contraindication to at least one conventional therapy option (see Appendix A).
3. Authorization of 12 months may be granted for the treatment of fistulizing CD.

B) Moderately to severely active ulcerative colitis (UC)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic drug (e.g. Xeljanz) indicated for moderately to severely active ulcerative colitis.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active UC for members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix B).
3. Authorization of 12 months may be granted for members who have been hospitalized for acute severe UC (e.g., continuous bleeding, severe toxic symptoms, including fever and anorexia).

C) Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Remicade, Inflectra, Renflexis, or Avsola must be

prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide.

2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   a.) Member is prescribed Remicade, Inflectra, Renflexis, or Avsola in combination with methotrexate or leflunomide, or has a clinical reason not to use methotrexate or leflunomide.
   b.) Member meets any of the following criteria:
      i). Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      ii). Member has an intolerance or contraindication to methotrexate (see Appendix C).

D) Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or axial spondyloarthritis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis or axial spondyloarthritis when any of the following criteria is met:
   a.) Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   b.) Member has an intolerance or contraindication to two or more NSAIDs (see Appendix D).

E) Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

F) Chronic severe plaque psoriasis

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of chronic severe plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of chronic severe plaque psoriasis when all of the following criteria are met:
   a.) At least 3% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b.) Member meets any of the following criteria:
      i). Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii). Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix E).
      iii). Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

G) Behçet's disease

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of Behçet's disease.
2. Authorization of 12 months may be granted for the treatment of Behçet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behçet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

H) Granulomatosis with polyangiitis (Wegener's granulomatosis)

Authorization of 12 months may be granted for treatment of granulomatosis with polyangiitis when either of the following criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressants (e.g., cyclophosphamide, azathioprine, methotrexate, or mycophenolate mofetil).

2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy.

I) Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of severe, refractory hidradenitis suppurativa.
2. Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa when either of the following is met:
    a. Member has experienced an inadequate response to oral antibiotics for at least 90 days.
    b. Member has an intolerance or contraindication to oral antibiotics.

J) Juvenile Idiopathic arthritis (JIA)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for the treatment of JIA when any of the following criteria is met:
    a.) Member has an inadequate response to at least a 1-month trial of NSAIDs.
    b.) Member has an inadequate response to at least a 2-week trial of corticosteroids.
    c.) Member has an inadequate response to at least a 3-month trial of methotrexate or leflunomide.

K) Pyoderma gangrenosum

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for pyoderma gangrenosum.
2. Authorization of 12 months may be granted for the treatment of pyoderma gangrenosum when either of the following is met:
    a.) Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).
    b.) Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).

L) Sarcoidosis

Authorization of 12 months may be granted for treatment of sarcoidosis in members when any of the following criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressants
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy.

M) Takayasu's arteritis

Authorization of 12 months may be granted for treatment of refractory Takayasu's arteritis when any of the following criteria is met:

1. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
2. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

N) Uveitis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for uveitis.
2. Authorization of 12 months may be granted for the treatment of uveitis when any of the following is met:

a.) Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
b.) Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

O) Reactive arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for reactive arthritis.
2. Authorization of 12 months may be granted for the treatment of reactive arthritis when any of the following criteria is met:
   a.) Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   b.) Member has an intolerance or contraindication to methotrexate (see Appendix C).

P) Immune Checkpoint Inhibitor Toxicity

1. Authorization of 1 month may be granted for the treatment of immune checkpoint inhibitor (e.g., CTLA-4, PD-1 inhibitor, or PD-L1 inhibitor) toxicity when all the following criteria are met:
   a) Member has recently received treatment with immune checkpoint inhibitor therapy (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, darvalumab)
   b) Member has experienced one or more of the following immune checkpoint inhibitor toxicities:
      - Moderate (Grade 2) or severe diarrhea and colitis (Grade 3-4)
      - Severe pneumonitis (Grade 3-4)
      - Severe or life-threatening renal failure and elevated serum creatinine (Grade 3-4)
      - Life-threatening myocarditis, pericarditis, arrhythmias, or impaired ventricular function (Grade 4)
      - Severe inflammatory arthritis with joint symptoms that are limiting the member's activities of daily living
   c) Member has experienced an inadequate response, intolerance, or contraindication to an adequate trial of systemic corticosteroid treatment

Continuation of Therapy

A) Immune Checkpoint Inhibitor Toxicity

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

B) All other indications

Authorization of 12 months may be granted for all members (including new members) who are using Remicade, Inflectra, Renflexis, or Avsola for an indication outlined in the initial authorization criteria and who achieve or maintain positive clinical response with Remicade, Inflectra, Renflexis, or Avsola as evidenced by low disease activity or improvement in signs and symptoms of the condition.

Other

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer infliximab to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of infliximab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use infliximab concomitantly with any other biologic DMARD or targeted synthetic DMARD.

Note: Members who have received Remicade, Inflectra, Renflexis, Avsola or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

Remicade, Inflectra, Renflexis and Avsola are considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Appendix

Appendix A: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Apriso, Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine

3. Severe disease – induction of remission:
    a. Prednisone, hydrocortisone IV, methylprednisolone IV
    b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
    a. Azathioprine, mercaptopurine
    b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
    a. Alternative: rectal mesalamine

Appendix C: Examples of Contraindications to Methotrexate or Leflunomide

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or currently planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix D: Examples of Contraindications to the Use of NSAIDs

1. Allergic-type reaction following aspirin or other NSAID administration
2. Asthma
3. Gastrointestinal bleeding
4. History of intolerance or adverse event
5. Significant drug interaction
6. Urticaria

Appendix E: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Clincal diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J1745 Injection infliximab, 10 mg (applies to Remicade product only; not biosimilars)
- Q5102 Injection infliximab, biosimilar - 10mg (cancelled 4/1/2018)
- Q5103 Injection infliximab, biosimilar - Inflectra, 10mg (new code effective 4/1/2018)
- Q5104 Injection infliximab, biosimilar - Renflexis, 10mg (new code effective 4/1/2018)
- Q5109 Injection, infliximab, biosimilar - Ixifi, 10 mg (new code effective 1/1/2019)
- Q5121 Injection, infliximab-axxq, biosimilar, (Avsola), 10 mg (new code effective 7/1/20)

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POLICY HISTORY

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