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), Avsola (infliximab-axxq), and Zymfentra (infliximab-dyyb). For this program, Avsola and Inflectra are the preferred products. Coverage for non-preferred products, Renflexis and Remicade (infliximab), is provided based on clinical circumstances that would exclude the use of the preferred products 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. Additionally for this program, Adalimumab-aacf, Enbrel, Entyvio, Cosentyx, Otezla, Otulfi (ustekinumab-aauz), Rinvoq, Simponi, Skyrizi, Tremfya, Velsipity and Xeljanz/Xeljanz XR are the preferred products and will apply to members requesting treatment with Zymfentra (infliximab-dyyb) and self-administered for an indication that is FDA-approved for the preferred product. The criteria will require the use of two of the health plan’s preferred products before the use of non-preferred products unless there are clinical circumstances that exclude the use of all the preferred products, the patient is currently receiving treatment with the non-preferred drug and experience a positive therapeutic outcome, or there is only one preferred product for an indication.

FDA-Approved Indications
Avsola, Inflectra, infliximab, Remicade, Renflexis

1. Adult patients with moderately to severely active Crohn’s disease (CD) and fistulizing CD who have had an inadequate response to conventional therapy
2. Pediatric patients 6 years of age and older with moderately to severely active Crohn’s disease who have had an inadequate response to conventional therapy

3. Moderately to severely active ulcerative colitis (UC) in patients 6 years of age or older who have had an inadequate response to conventional therapy
4. Adult patients with moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
5. Adult patients with active ankylosing spondylitis (AS)
6. Adult patients with active psoriatic arthritis (PsA)
7. Adult patients with chronic severe plaque psoriasis (PsO) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate

Zymfentra

1. Maintenance treatment of moderately to severely active ulcerative colitis in adults following treatment with an infliximab product administered intravenously
2. Maintenance treatment of moderately to severely active Crohn's disease in adults following treatment with an infliximab product administered intravenously

Compendial Uses (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

1. Non-radiographic 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-related toxicity
12. Acute graft versus host disease
13. Moderate to severe plaque psoriasis

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

A. Crohn's disease (CD)
   1. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

B. Ulcerative colitis (UC)
   1. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

C. Rheumatoid arthritis (RA)
   1. Initial requests:
      i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
      ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. Ankylosing spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA),reactive arthritis, hidradenitis suppurativa, and uveitis:
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

E. Plaque psoriasis (PsO)
   1. Initial requests:
      i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
      ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms.

F. Behçet's disease (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).

G. Granulomatosis with polyangiitis (Wegener's granulomatosis), Pyoderma gangrenosum, sarcoidosis, Takayasu's arteritis, immune checkpoint inhibitor related toxicity, and acute graft versus host disease (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

H. Juvenile Idiopathic Arthritis (JIA):
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

<u>Prescriber Specialties (initial approvals only)</u>

The medication must be prescribed by or in consultation with one of the following:

A. Crohn's disease and ulcerative colitis: gastroenterologist
B. Rheumatoid arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, juvenile idiopathic arthritis, Behçet's disease, Takayasu's arteritis, and reactive arthritis: rheumatologist
C. Psoriatic arthritis and hidradenitis suppurativa: rheumatologist or dermatologist
D. Plaque psoriasis and pyoderma gangrenosum: dermatologist
E. Granulomatosis with polyangiitis: rheumatologist, nephrologist, pulmonologist or otolaryngologist
F. Sarcoidosis: dermatologist, pulmonologist, rheumatologist, cardiologist, neurologist, or ophthalmologist
G. Uveitis: ophthalmologist or rheumatologist
H. Immune checkpoint inhibitor related inflammatory arthritis: oncologist, hematologist, or rheumatologist
I. Immune checkpoint inhibitor related toxicity: gastroenterologist, oncologist or hematologist
J. Acute graft versus host disease: oncologist or hematologist

<u>Preferred Drug Plan Design</u>

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

Remicade (infliximab) and Renflexis

A. Coverage for a non-preferred product is provided when the member has a documented intolerable adverse event to all the preferred products, Avsola and Inflectra, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the reference product and biosimilar products).

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

	Products
Preferred	**Avsola** (infliximab-axxq) **Inflectra** (infliximab-dyyb)
Targeted	**Remicade** (infliximab) **Renflexis** (infliximab-abda)

Zymfentra

A. Criteria for initial approval for **ulcerative colitis** will only apply when the member has had an inadequate response to treatment or intolerable adverse event with at least TWO of the preferred products (Adalimumab-aacf, Entyvio, Otulfi (ustekinumab-aauz), Rinvoq, Simponi, Skyrizi, Tremfya, Velsipity and Xeljanz/Xeljanz XR).

B. Criteria for initial approval for **Crohn's disease** will only apply when the member has had an inadequate response to treatment or intolerable adverse event with at least TWO of the preferred products (Adalimumab-aacf, Entyvio, Otulfi (ustekinumab-aauz), Rinvoq, Skyrizi, and Tremfya).

Criteria for Initial Approval

A) Crohn's disease (CD)

1. Avsola, Inflectra, infliximab, Remicade, Renflexis
    a. Authorization of 12 months may be granted for treatment of moderately to severely active CD.

2. Zymfentra
    a. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active CD.

B) Ulcerative colitis (UC)

1. Avsola, Inflectra, infliximab, Remicade, Renflexis
    a. Authorization of 12 months may be granted for the treatment of moderately to severely active UC.

2. Zymfentra
    a. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active UC.

C) Rheumatoid arthritis (RA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis. The requested medication must be prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide (see Appendix A).
2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following criteria are met:

i. Member meets either of the following criteria:
    a. Member has been tested for either of the following biomarkers and the test was positive:
        1. Rheumatoid factor (RF)
        2. Anti-cyclic citrullinated peptide (anti-CCP)
    b. Member has been tested for ALL of the following biomarkers:
        1. RF
        2. Anti-CCP
        3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
ii. Member is prescribed the requested medication in combination with methotrexate or leflunomide or has a clinical reason not to use methotrexate or leflunomide (see Appendix A).
iii. Member meets any of the following criteria:
    a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
    b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

D) Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for active ankylosing spondylitis or active non-radiographic axial spondyloarthritis.
2. Authorization of 12 months may be granted for adult members for treatment of active ankylosing spondylitis or active non-radiographic axial spondyloarthritis when any of the following criteria is met:
    i. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
    ii. Member has an intolerance or contraindication to two or more NSAIDs.

E) Psoriatic arthritis (PsA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Otezla) indicated for active psoriatic arthritis.
2. Authorization of 12 months may be granted for adult members for treatment of active psoriatic arthritis when either of the following criteria is met:
    i. Member has mild to moderate disease and meets one of the following criteria:
        a. Member has had an inadequate response to methotrexate, leflunomide, or another conventional synthetic drug (e.g., sulfasalazine) administered at an adequate dose and duration.
        b. Member has an intolerance or contraindication to methotrexate or leflunomide (see Appendix A), or another conventional synthetic drug (e.g., sulfasalazine).
        c. Member has enthesitis or predominantly axial disease.
    ii. Member has severe disease.

F) Plaque psoriasis (PsO) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Sotyktu, Otezla) indicated for the treatment of moderate to severe plaque psoriasis.
2. Authorization of 12 months may be granted for adult members for treatment of moderate to severe plaque psoriasis in members when any of the following criteria is met:
    i. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.

ii. At least 10% of the body surface area (BSA) is affected.
iii. At least 3% of body surface area (BSA) is affected and the member meets any of the following criteria:
    a. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
    b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix A).

G) Behçet's disease (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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 non-biologic medication for Behçet's disease (e.g., azathioprine, colchicine, cyclosporine, systemic corticosteroids).

H) Granulomatosis with polyangiitis (Wegener's granulomatosis) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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

I) Hidradenitis suppurativa (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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:
    i. Member has experienced an inadequate response to an oral antibiotic used for the treatment of hidradenitis suppurativa (e.g., clindamycin, metronidazole, moxifloxacin, rifampin, tetracyclines) for at least 90 days.
    ii. Member has an intolerance or contraindication to oral antibiotics used for the treatment of hidradenitis suppurativa.

J) Juvenile idiopathic arthritis (JIA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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 juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for the treatment of JIA when any of the following criteria is met:
    i. Member has an inadequate response to methotrexate or another conventional synthetic drug (e.g., leflunomide, sulfasalazine, hydroxychloroquine) administered at an adequate dose and duration.
    ii. Member has an inadequate response to a trial of scheduled non-steroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids (e.g., triamcinolone hexacetonide) and one of the following risk factors for poor outcome:
        a. Involvement of ankle, wrist, hip, sacroiliac joint, and/or temporomandibular joint (TMJ)
        b. Presence of erosive disease or enthesitis
        c. Delay in diagnosis
        d. Elevated levels of inflammation markers
        e. Symmetric disease

iii. Member has risk factors for disease severity and potentially a more refractory disease course (see Appendix B) and the member also meets one of the following:
    a. High-risk joints are involved (e.g., cervical spine, wrist, or hip)
    b. High disease activity
    c. Are judged to be at high risk for disabling joint disease.

K) Pyoderma gangrenosum (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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 treatment of pyoderma gangrenosum when either of the following is met:
    i. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., cyclosporine, or mycophenolate mofetil).
    ii. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., cyclosporine, mycophenolate mofetil).

L) Sarcoidosis (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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

M) Takayasu's arteritis (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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 (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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 treatment of uveitis when any of the following criteria is met:
    i. Member has experienced an inadequate response to corticosteroids or immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).
    ii. Member has an intolerance or contraindication to corticosteroids and immunosuppressive therapy (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

O) Reactive arthritis (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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 treatment of reactive arthritis when any of the following criteria is met:
    i. Member has experienced an inadequate response to at least a 3-month trial of one of the following despite adequate dosing or maximally tolerated dose:
        a. Sulfasalazine (i.e., titrated to 1000 mg twice daily)
        b. Methotrexate (i.e., titrated to at least 15 mg/week)

ii. Member has an intolerance or contraindication to methotrexate (see Appendix A) and sulfasalazine (e.g., porphyria, intestinal or urinary obstruction).

P) Immune checkpoint inhibitor related toxicity (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

1. Authorization of 6 months may be granted for treatment of immune checkpoint inhibitor toxicity when the member has experienced and inadequate response, intolerance or contraindication to corticosteroids.
2. Authorization of 12 months may be granted for treatment of immune checkpoint inhibitor toxicity when the member has moderate or severe inflammatory arthritis and has experienced an inadequate response, intolerance, or contraindication to corticosteroids.

Q) Acute graft versus host disease (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

1. Authorization of 12 months may be granted for treatment of acute graft versus host disease when either of the following criteria is met:
   i. Member has experienced an inadequate response to systemic corticosteroids
   ii. Member has an intolerance or contraindication to corticosteroids

Continuation of Therapy

A) Crohn's disease (CD)

1. Authorization of 12 months may be granted for all members (adult members for Zymfentra requests) (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all members (adult members for Zymfentra requests) (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
   i. Abdominal pain or tenderness
   ii. Diarrhea
   iii. Body weight
   iv. Abdominal mass
   v. Hematocrit
   vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
   vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

B) Ulcerative colitis (UC)

1. Authorization of 12 months may be granted for all members (adult members for Zymfentra requests) (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain remission.

2. Authorization of 12 months may be granted for all members (adult members for Zymfentra requests) (including new members) who are using the requested medication for moderately to severely active ulcerative colitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and

symptoms of the condition when there is improvement in any of the following from baseline:

i. Stool frequency
ii. Rectal bleeding
iii. Urgency of defecation
iv. C-reactive protein (CRP)
v. Fecal calprotectin (FC)
vi. Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)

C) Rheumatoid arthritis (RA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

D) Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for ankylosing spondylitis or non-radiographic axial spondyloarthritis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g., morning stiffness)
4. Swollen joints
5. Tender joints
6. C-reactive protein (CRP)

E) Psoriatic arthritis (PsA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Axial disease
6. Skin and/or nail involvement
7. Functional status
8. C-reactive protein (CRP)

F) Plaque psoriasis (PsO) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in body surface area (BSA) affected from baseline

2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

G) Hidradenitis suppurativa (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for severe, refractory hidradenitis suppurativa and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in abscess and inflammatory nodule count from baseline
2. Reduced formation of new sinus tracts and scarring
3. Decrease in frequency of inflammatory lesions from baseline
4. Reduction in pain from baseline
5. Reduction in suppuration from baseline
6. Improvement in frequency of relapses from baseline
7. Improvement in quality of life from baseline
8. Improvement on a disease severity assessment tool from baseline

H) Juvenile idiopathic arthritis (JIA) (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

I) Uveitis (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for uveitis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when the patient meets any of the following:

1. Reduced frequency of flare recurrence compared to baseline
2. Zero anterior chamber inflammation or reduction in anterior chamber inflammation compared to baseline
3. Decreased reliance on topical corticosteroids

J) Reactive arthritis (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for reactive arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition (e.g., tender joint count, swollen joint count, or pain).

K) Immune checkpoint inhibitor related toxicity and acute graft versus host disease (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

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

L) All other indications (Avsola, Inflectra, infliximab, Remicade, Renflexis only)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined in the initial authorization criteria and

who achieve or maintain positive clinical response with the requested medication 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 tuberculosis (TB) test (which can include a tuberculosis skin test [TST]or an interferon-release assay [IGRA])* within 12 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease (e.g., chest x-ray). Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug for the same indication.

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

Members currently receiving Zymfentra as samples or via the manufacturer's patient assistance program will be required to meet the criteria for initial approval. This ensures that members are treated equally regardless of their provider's ability to access medication samples.

Non-Formulary Exception Criteria

Non-Formulary Exception criteria applies to formularies which do not include the requested product(s) on the formulary drug list. Meeting the criteria above may satisfy some, or all, portions of the Non-Formulary Exception Criteria. A medication that is non-formulary may be covered when the Criteria for Approval AND the following criteria are met:

1. The requested drug must be used for an FDA-approved indication, or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines). Diagnostic testing/lab results required when applicable.
2. The prescribed dose/quantity must fall within the FDA-approved labeling or dosing guidelines found in the compendia of current literature.
3. All covered formulary alternative drugs on any tier will be ineffective, have been ineffective, would not be as effective as the non-formulary drug, or would have adverse effects. Documentation is required and must include chart note(s) or other documentation indicating prior treatment failure, severity of the adverse event (if any), and dosage and duration of the prior treatment, or contraindication to formulary alternatives.

Dosage and Administration

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

Quantity Limits Apply (Zymfentra only)

Medication	Standard Limit	FDA Recommended Dosing
Zymfentra (infliximab-dyyb) 120 mg/mL Prefilled Syringe	2 pens/syringes per 28 days	Inject 120 mg subcutaneously once every two weeks
Zymfentra (infliximab-dyyb) 120 mg/mL Prefilled Syringe with Needle Guard		

Zymfentra (infliximab-dyyb) 120 mg/mL Prefilled Pen		

Appendices

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

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

Appendix B: Risk factors for Juvenile Idiopathic Arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

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)
- J1748 Injection, infliximab-dyyb (zymfentra), 10 mg (effective 7/1/2024)
- 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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