Infliximab (Avsola, Inflectra, Remicade, Renflexis, & Zymfentra)

Policy Number: MC/PC 021
Effective Date: November 1, 2025

Table of Contents **Page**

Coverage Rationale 1
Applicable Codes 4
Background 14
Clinical Evidence 14
U.S. Food and Drug Administration 233
References 24
Policy History/Revision Information 25
Instructions for Use 25

Related Policies

- n/a

Coverage Rationale

<Please refer to Medical Benefit Plan Sponsor for preferred medications. Preferred products may be updated and therefore subject to change>.

This policy refers to the following infliximab products:

- Remicade (infliximab) for injection, for intravenous use
- Avsola (infliximab-axxq) for injection, for intravenous use
- Inflectra (infliximab-dyyb) for injection, for intravenous use
- Renflexis (infliximab-abda) for injection, for intravenous use
- Zymfentra (infliximab-dyyb) injection, for subcutaneous use

Ankylosing Spondylitis

For initial coverage of infliximab for Ankylosing Spondylitis (AS), the following will be required:

- Diagnosis of active ankylosing spondylitis **and**
- Prescribed by or in consultation with a rheumatologist. **and**
- Minimum duration of one month trial and failure, contraindication, or intolerance to two different NSAIDs (e.g., ibuprofen, naproxen) at maximally tolerated doses.

For reauthorization coverage of infliximab for Ankylosing Spondylitis (AS), the following will be required:

- Presence of positive clinical response to therapy as evidenced by improvement from baseline for at least one of the following:
  - Disease activity (e.g., pain, fatigue, inflammation, stiffness)
  - Lab values (erythrocyte sedimentation rate, C-reactive protein level)

- Function
- Axial status (e.g., lumbar spine motion, chest expansion)
- Total active (swollen and tender) joint count

Crohn's Disease/Fistulizing Crohn's Disease

For initial coverage of IV infliximab for Crohn's Disease (CD) or Fistulizing Crohn's Disease, the following will be required:

- One of the following diagnoses:
  - Moderately to severely active Crohn's disease
  - Fistulizing Crohn's disease **and**
- One of the following:
  - Frequent diarrhea and abdominal pain
  - At least 10% weight loss
  - Complications such as obstruction, fever, abdominal mass
  - Abnormal lab values (e.g., C-reactive protein [CRP])
  - CD Activity Index (CDAI) greater than 220 **and**
- Prescribed by or in consultation with a gastroenterologist **and**
- Trial and failure, contraindication, or intolerance to one of the following conventional therapies:
  - 6-mercaptopurine
  - Azathioprine
  - Corticosteroids (e.g., prednisone)
  - Methotrexate

For initial coverage of Zymfentra for Crohn's Disease (CD) or Fistulizing Crohn's Disease, the following will be required:

- Diagnosis of moderately to severely active Crohn's disease **and**
- Patient has achieved a clinical response following a minimum of 10 weeks of IV infliximab **and**
- Provider attests that continued IV administration is not appropriate for the patient (e.g., problems with IV access) **and**
- Prescribed by or in consultation with a gastroenterologist

For reauthorization coverage of infliximab for Crohn's Disease (CD) or Fistulizing Crohn's Disease, the following will be required:

- Presence of positive clinical response to therapy as evidenced by at least one of the following:
  - Improvement in intestinal inflammation (e.g., mucosal healing, improvement of lab values [platelet counts, erythrocyte sedimentation rate, C-reactive protein level]) from baseline.
  - Reversal of high fecal output state

Rheumatoid Arthritis

For initial coverage of infliximab for Rheumatoid Arthritis (RA), the following will be required:

- Diagnosis of moderately to severely active RA **and**
- Prescribed by or in consultation with a rheumatologist **and**
- Minimum duration of a 3-month trial and failure, contraindication, or intolerance to one of the following conventional therapies at maximally tolerated doses:
  - methotrexate
  - leflunomide
  - sulfasalazine **and**
- Used in combination with methotrexate.

For reauthorization coverage of infliximab for Rheumatoid Arthritis (RA), the following will be required:

- Presence of positive clinical response to therapy as evidenced by at least one of the following:
  - Reduction in the total active (swollen and tender) joint count from baseline
  - Improvement in symptoms (e.g., pain, stiffness, inflammation) from baseline

Plaque Psoriasis

For initial coverage of infliximab for Plaque Psoriasis (PsO), the following will be required:

- Diagnosis of chronic severe (i.e., extensive and/or disabling) plaque **and**
- One of the following:
  - Greater than or equal to 3% body surface area involvement
  - Severe scalp psoriasis
  - Palmoplantar (i.e., palms, soles), facial, or genital involvement **and**
- Trial and failure of a minimum 30-day supply (14-day supply for topical corticosteroids), contraindication, or intolerance to one of the following topical therapies:
  - corticosteroids (e.g., betamethasone, clobetasol)
  - vitamin D analogs (e.g., calcitriol, calcipotriene)
  - tazarotene
  - calcineurin inhibitors (e.g., tacrolimus, pimecrolimus) **and**
- Prescribed by or in consultation with a dermatologist.

For reauthorization coverage of infliximab for Plaque Psoriasis (PsO), the following will be required:

- Presence of positive clinical response to infliximab therapy as evidenced by ONE of the following:
  - Reduction in the body surface area (BSA) involvement from baseline
  - Improvement in symptoms (e.g., pruritus, inflammation) from baseline

Psoriatic Arthritis

For initial coverage of infliximab for Psoriatic Arthritis (PsA), the following will be required:

- Diagnosis of active PsA **and**
- One of the following:
  - Actively inflamed joints
  - Dactylitis
  - Enthesitis
  - Axial disease
  - Active skin and/or nail involvement **and**
- Prescribed by or in consultation with one of the following:
  - Dermatologist
  - Rheumatologist

For reauthorization coverage of infliximab for Psoriatic Arthritis (PsA), the following will be required:

- Presence of positive clinical response to therapy as evidenced by at least one of the following:
  - Reduction in the total active (swollen and tender) joint count from baseline
  - Improvement in symptoms (e.g., pain, stiffness, pruritus, inflammation) from baseline
  - Reduction in the body surface area (BSA) involvement from baseline

Sarcoidosis

For initial coverage of infliximab for Sarcoidosis [Off-label], the following will be required:

- Diagnosis of sarcoidosis **and**

- Prescribed by or in consultation with one of the following:
    - Pulmonologist
    - Dermatologist
    - Ophthalmologist **and**
- Trial and failure, contraindication, or intolerance to one corticosteroid (e.g., prednisone) **and**
- Trial and failure, contraindication, or intolerance to one immunosuppressant (e.g., methotrexate, cyclophosphamide, or azathioprine)

For reauthorization coverage of infliximab for Sarcoidosis [Off-label], the following will be required:

- Presence of positive clinical response to infliximab therapy

Ulcerative Colitis

For initial coverage of IV infliximab for Ulcerative Colitis (UC), the following will be required:

- Diagnosis of moderately to severely active ulcerative colitis **and**
- One of the following:
    - Greater than 6 stools per day
    - Frequent blood in the stools
    - Frequent urgency
    - Presence of ulcers
    - Abnormal lab values (e.g., hemoglobin, ESR, CRP)
    - Dependent on, or refractory to, corticosteroids **and**
- Prescribed by or in consultation with a gastroenterologist **and**
- Trial and failure, contraindication, or intolerance to one of the following conventional therapies:
    - 6-mercaptopurine
    - Aminosalicylate (e.g., mesalamine, olsalazine, sulfasalazine)
    - Azathioprine
    - Corticosteroids (e.g., prednisone)

For initial coverage of Zymfentra for Ulcerative Colitis (UC), the following will be required:

- Diagnosis of moderately to severely active ulcerative colitis **and**
- Patient has achieved a clinical response following a minimum of 10 weeks of IV infliximab **and**
- Provider attests that continued IV administration is not appropriate for the patient (e.g., problems with IV access) **and**
- Prescribed by or in consultation with a gastroenterologist

For reauthorization coverage of infliximab for Ulcerative Colitis (UC), the following will be required:

- Presence of positive clinical response to therapy as evidenced by at least one of the following:
    - Improvement in intestinal inflammation (e.g., mucosal healing, improvement of lab values [platelet counts, erythrocyte sedimentation rate, C-reactive protein level]) from baseline
    - Reversal of high fecal output state

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1745	Injection, infliximab, excludes biosimilar, 10 mg
J1748	Injection, infliximab-dyyb (Zymfentra), 10 mg
Q5121	Injection, infliximab-axxq, biosimilar, (Avsola), 10 mg
Q5103	Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg

ICD-10 Code	Description
D86.0	Sarcoidosis of lung
D86.1	Sarcoidosis of lymph nodes
D86.2	Sarcoidosis of lung with sarcoidosis of lymph nodes
D86.3	Sarcoidosis of skin
D86.81	Sarcoid meningitis
D86.82	Multiple cranial nerve palsies in sarcoidosis
D86.83	Sarcoid iridocyclitis
D86.84	Sarcoid pyelonephritis
D86.85	Sarcoid myocarditis
D86.86	Sarcoid arthropathy
D86.87	Sarcoid myositis
D86.89	Sarcoidosis of other sites
D86.9	Sarcoidosis, unspecified
K50.00	Crohn's disease of small intestine without complications
K50.011	Crohn's disease of small intestine with rectal bleeding
K50.012	Crohn's disease of small intestine with intestinal obstruction
K50.013	Crohn's disease of small intestine with fistula
K50.014	Crohn's disease of small intestine with abscess
K50.018	Crohn's disease of small intestine with other complication
K50.019	Crohn's disease of small intestine with unspecified complications
K50.10	Crohn's disease of large intestine without complications
K50.111	Crohn's disease of large intestine with rectal bleeding
K50.112	Crohn's disease of large intestine with intestinal obstruction
K50.113	Crohn's disease of large intestine with fistula
K50.114	Crohn's disease of large intestine with abscess
K50.118	Crohn's disease of large intestine with other complication
K50.119	Crohn's disease of large intestine with unspecified complications
K50.80	Crohn's disease of both small and large intestine without complications
K50.811	Crohn's disease of both small and large intestine with rectal bleeding
K50.812	Crohn's disease of both small and large intestine with intestinal obstruction
K50.813	Crohn's disease of both small and large intestine with fistula
K50.814	Crohn's disease of both small and large intestine with abscess

ICD-10 Code	Description
K50.818	Crohn's disease of both small and large intestine with other complication
K50.819	Crohn's disease of both small and large intestine with unspecified complications
K50.90	Crohn's disease, unspecified, without complications
K50.911	Crohn's disease, unspecified, with rectal bleeding
K50.912	Crohn's disease, unspecified, with intestinal obstruction
K50.913	Crohn's disease, unspecified, with fistula
K50.914	Crohn's disease, unspecified, with abscess
K50.918	Crohn's disease, unspecified, with other complication
K50.919	Crohn's disease, unspecified, with unspecified complications
K51.00	Ulcerative (chronic) pancolitis without complications
K51.011	Ulcerative (chronic) pancolitis with rectal bleeding
K51.012	Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013	Ulcerative (chronic) pancolitis with fistula
K51.014	Ulcerative (chronic) pancolitis with abscess
K51.018	Ulcerative (chronic) pancolitis with other complication
K51.019	Ulcerative (chronic) pancolitis with unspecified complications
K51.20	Ulcerative (chronic) proctitis without complications
K51.211	Ulcerative (chronic) proctitis with rectal bleeding
K51.212	Ulcerative (chronic) proctitis with intestinal obstruction
K51.213	Ulcerative (chronic) proctitis with fistula
K51.214	Ulcerative (chronic) proctitis with abscess
K51.218	Ulcerative (chronic) proctitis with other complication
K51.219	Ulcerative (chronic) proctitis with unspecified complications
K51.30	Ulcerative (chronic) rectosigmoiditis without complications
K51.311	Ulcerative (chronic) rectosigmoiditis with rectal bleeding
K51.312	Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313	Ulcerative (chronic) rectosigmoiditis with fistula
K51.314	Ulcerative (chronic) rectosigmoiditis with abscess
K51.318	Ulcerative (chronic) rectosigmoiditis with other complication
K51.319	Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.50	Left sided colitis without complications
K51.511	Left sided colitis with rectal bleeding
K51.512	Left sided colitis with intestinal obstruction
K51.513	Left sided colitis with fistula
K51.514	Left sided colitis with abscess
K51.518	Left sided colitis with other complication
K51.519	Left sided colitis with unspecified complications
K51.80	Other ulcerative colitis without complications
K51.811	Other ulcerative colitis with rectal bleeding

ICD-10 Code	Description
K51.812	Other ulcerative colitis with intestinal obstruction
K51.813	Other ulcerative colitis with fistula
K51.814	Other ulcerative colitis with abscess
K51.818	Other ulcerative colitis with other complication
K51.819	Other ulcerative colitis with unspecified complications
K51.90	Ulcerative colitis, unspecified, without complications
K51.911	Ulcerative colitis, unspecified with rectal bleeding
K51.912	Ulcerative colitis, unspecified with intestinal obstruction
K51.913	Ulcerative colitis, unspecified with fistula
K51.914	Ulcerative colitis, unspecified with abscess
K51.918	Ulcerative colitis, unspecified with other complication
K51.919	Ulcerative colitis, unspecified with unspecified complications
K63.2	Fistula of intestine
L40.0	Psoriasis vulgaris
L40.1	Generalized pustular psoriasis
L40.2	Acrodermatitis continua
L40.3	Pustulosis palmaris et plantaris
L40.4	Guttate psoriasis
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis
L40.54	Psoriatic juvenile arthropathy
L40.59	Other psoriatic arthropathy
L40.8	Other psoriasis
L40.9	Psoriasis, unspecified
L73.2	Hidradenitis suppurativa
M05.20	Rheumatoid vasculitis with rheumatoid arthritis of unspecified site
M05.211	Rheumatoid vasculitis with rheumatoid arthritis of right shoulder
M05.212	Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.219	Rheumatoid vasculitis with rheumatoid arthritis of unspecified shoulder
M05.221	Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222	Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.229	Rheumatoid vasculitis with rheumatoid arthritis of unspecified elbow
M05.231	Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232	Rheumatoid vasculitis with rheumatoid arthritis of left wrist
M05.239	Rheumatoid vasculitis with rheumatoid arthritis of unspecified wrist
M05.241	Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242	Rheumatoid vasculitis with rheumatoid arthritis of left hand

ICD-10 Code	Description
M05.249	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hand
M05.251	Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252	Rheumatoid vasculitis with rheumatoid arthritis of left hip
M05.259	Rheumatoid vasculitis with rheumatoid arthritis of unspecified hip
M05.261	Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262	Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.269	Rheumatoid vasculitis with rheumatoid arthritis of unspecified knee
M05.271	Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272	Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot
M05.279	Rheumatoid vasculitis with rheumatoid arthritis of unspecified ankle and foot
M05.29	Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.30	Rheumatoid heart disease with rheumatoid arthritis of unspecified site
M05.311	Rheumatoid heart disease with rheumatoid arthritis of right shoulder
M05.312	Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.319	Rheumatoid heart disease with rheumatoid arthritis of unspecified shoulder
M05.321	Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322	Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.329	Rheumatoid heart disease with rheumatoid arthritis of unspecified elbow
M05.331	Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332	Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.339	Rheumatoid heart disease with rheumatoid arthritis of unspecified wrist
M05.341	Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342	Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.349	Rheumatoid heart disease with rheumatoid arthritis of unspecified hand
M05.351	Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352	Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.359	Rheumatoid heart disease with rheumatoid arthritis of unspecified hip
M05.361	Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362	Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.369	Rheumatoid heart disease with rheumatoid arthritis of unspecified knee
M05.371	Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372	Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.379	Rheumatoid heart disease with rheumatoid arthritis of unspecified ankle and foot
M05.39	Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.40	Rheumatoid myopathy with rheumatoid arthritis of unspecified site
M05.411	Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412	Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.419	Rheumatoid myopathy with rheumatoid arthritis of unspecified shoulder
M05.421	Rheumatoid myopathy with rheumatoid arthritis of right elbow

ICD-10 Code	Description
M05.422	Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.429	Rheumatoid myopathy with rheumatoid arthritis of unspecified elbow
M05.431	Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432	Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.439	Rheumatoid myopathy with rheumatoid arthritis of unspecified wrist
M05.441	Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442	Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.449	Rheumatoid myopathy with rheumatoid arthritis of unspecified hand
M05.451	Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452	Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.459	Rheumatoid myopathy with rheumatoid arthritis of unspecified hip
M05.461	Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462	Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.469	Rheumatoid myopathy with rheumatoid arthritis of unspecified knee
M05.471	Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472	Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.479	Rheumatoid myopathy with rheumatoid arthritis of unspecified ankle and foot
M05.49	Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.50	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site
M05.511	Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512	Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder
M05.519	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified shoulder
M05.521	Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522	Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow
M05.529	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified elbow
M05.531	Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532	Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.539	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist
M05.541	Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542	Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.549	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand
M05.551	Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552	Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.559	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip
M05.561	Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562	Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.569	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee
M05.571	Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572	Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot

ICD-10 Code	Description
M05.579	Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot
M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.60	Rheumatoid arthritis of unspecified site with involvement of other organs and systems
M05.611	Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612	Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.619	Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems
M05.621	Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622	Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.629	Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems
M05.631	Rheumatoid arthritis of right wrist with involvement of other organs and systems
M05.632	Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.639	Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems
M05.641	Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642	Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.649	Rheumatoid arthritis of unspecified hand with involvement of other organs and systems
M05.651	Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652	Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.659	Rheumatoid arthritis of unspecified hip with involvement of other organs and systems
M05.661	Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662	Rheumatoid arthritis of left knee with involvement of other organs and systems
M05.669	Rheumatoid arthritis of unspecified knee with involvement of other organs and systems
M05.671	Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672	Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems
M05.679	Rheumatoid arthritis of unspecified ankle and foot with involvement of other organs and systems
M05.69	Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.70	Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement
M05.711	Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712	Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.719	Rheumatoid arthritis with rheumatoid factor of unspecified shoulder without organ or systems involvement
M05.721	Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722	Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.729	Rheumatoid arthritis with rheumatoid factor of unspecified elbow without organ or systems involvement
M05.731	Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732	Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement

ICD-10 Code	Description
M05.739	Rheumatoid arthritis with rheumatoid factor of unspecified wrist without organ or systems involvement
M05.741	Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742	Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.749	Rheumatoid arthritis with rheumatoid factor of unspecified hand without organ or systems involvement
M05.751	Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752	Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.759	Rheumatoid arthritis with rheumatoid factor of unspecified hip without organ or systems involvement
M05.761	Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762	Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement
M05.769	Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement
M05.771	Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement
M05.772	Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement
M05.779	Rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot without organ or systems involvement
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M05.80	Other rheumatoid arthritis with rheumatoid factor of unspecified site
M05.811	Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812	Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.819	Other rheumatoid arthritis with rheumatoid factor of unspecified shoulder
M05.821	Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822	Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.829	Other rheumatoid arthritis with rheumatoid factor of unspecified elbow
M05.831	Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832	Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.839	Other rheumatoid arthritis with rheumatoid factor of unspecified wrist
M05.841	Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842	Other rheumatoid arthritis with rheumatoid factor of left hand
M05.849	Other rheumatoid arthritis with rheumatoid factor of unspecified hand
M05.851	Other rheumatoid arthritis with rheumatoid factor of right hip
M05.852	Other rheumatoid arthritis with rheumatoid factor of left hip
M05.859	Other rheumatoid arthritis with rheumatoid factor of unspecified hip
M05.861	Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862	Other rheumatoid arthritis with rheumatoid factor of left knee

ICD-10 Code	Description
M05.869	Other rheumatoid arthritis with rheumatoid factor of unspecified knee
M05.871	Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872	Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.879	Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot
M05.89	Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.8A	Other rheumatoid arthritis with rheumatoid factor of other specified site
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M06.00	Rheumatoid arthritis without rheumatoid factor, unspecified site
M06.011	Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012	Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.019	Rheumatoid arthritis without rheumatoid factor, unspecified shoulder
M06.021	Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022	Rheumatoid arthritis without rheumatoid factor, left elbow
M06.029	Rheumatoid arthritis without rheumatoid factor, unspecified elbow
M06.031	Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032	Rheumatoid arthritis without rheumatoid factor, left wrist
M06.039	Rheumatoid arthritis without rheumatoid factor, unspecified wrist
M06.041	Rheumatoid arthritis without rheumatoid factor, right hand
M06.042	Rheumatoid arthritis without rheumatoid factor, left hand
M06.049	Rheumatoid arthritis without rheumatoid factor, unspecified hand
M06.051	Rheumatoid arthritis without rheumatoid factor, right hip
M06.052	Rheumatoid arthritis without rheumatoid factor, left hip
M06.059	Rheumatoid arthritis without rheumatoid factor, unspecified hip
M06.061	Rheumatoid arthritis without rheumatoid factor, right knee
M06.062	Rheumatoid arthritis without rheumatoid factor, left knee
M06.069	Rheumatoid arthritis without rheumatoid factor, unspecified knee
M06.071	Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072	Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.079	Rheumatoid arthritis without rheumatoid factor, unspecified ankle and foot
M06.08	Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.0A	Rheumatoid arthritis without rheumatoid factor, other specified site
M06.9	Rheumatoid arthritis, unspecified
M08.011	Unspecified juvenile rheumatoid arthritis, right shoulder
M08.012	Unspecified juvenile rheumatoid arthritis, left shoulder
M08.021	Unspecified juvenile rheumatoid arthritis, right elbow
M08.022	Unspecified juvenile rheumatoid arthritis, left elbow
M08.031	Unspecified juvenile rheumatoid arthritis, right wrist
M08.032	Unspecified juvenile rheumatoid arthritis, left wrist

ICD-10 Code	Description
M08.041	Unspecified juvenile rheumatoid arthritis, right hand
M08.042	Unspecified juvenile rheumatoid arthritis, left hand
M08.051	Unspecified juvenile rheumatoid arthritis, right hip
M08.052	Unspecified juvenile rheumatoid arthritis, left hip
M08.061	Unspecified juvenile rheumatoid arthritis, right knee
M08.062	Unspecified juvenile rheumatoid arthritis, left knee
M08.071	Unspecified juvenile rheumatoid arthritis, right ankle and foot
M08.072	Unspecified juvenile rheumatoid arthritis, left ankle and foot
M08.08	Unspecified juvenile rheumatoid arthritis, vertebrae
M08.09	Unspecified juvenile rheumatoid arthritis, multiple sites
M08.0A	Unspecified juvenile rheumatoid arthritis, other specified site
M08.1	Juvenile ankylosing spondylitis
M08.2A	Juvenile rheumatoid arthritis with systemic onset, other specified site
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.411	Pauciarticular juvenile rheumatoid arthritis, right shoulder
M08.412	Pauciarticular juvenile rheumatoid arthritis, left shoulder
M08.421	Pauciarticular juvenile rheumatoid arthritis, right elbow
M08.422	Pauciarticular juvenile rheumatoid arthritis, left elbow
M08.431	Pauciarticular juvenile rheumatoid arthritis, right wrist
M08.432	Pauciarticular juvenile rheumatoid arthritis, left wrist
M08.441	Pauciarticular juvenile rheumatoid arthritis, right hand
M08.442	Pauciarticular juvenile rheumatoid arthritis, left hand
M08.451	Pauciarticular juvenile rheumatoid arthritis, right hip
M08.452	Pauciarticular juvenile rheumatoid arthritis, left hip
M08.461	Pauciarticular juvenile rheumatoid arthritis, right knee
M08.462	Pauciarticular juvenile rheumatoid arthritis, left knee
M08.471	Pauciarticular juvenile rheumatoid arthritis, right ankle and foot
M08.472	Pauciarticular juvenile rheumatoid arthritis, left ankle and foot
M08.48	Pauciarticular juvenile rheumatoid arthritis, vertebrae
M08.9A	Juvenile arthritis, unspecified, other specified site
M31.4	Aortic arch syndrome [Takayasu]
M35.2	Behcet's disease
M45.0	Ankylosing spondylitis of multiple sites in spine
M45.1	Ankylosing spondylitis of occipito-atlanto-axial region
M45.2	Ankylosing spondylitis of cervical region
M45.3	Ankylosing spondylitis of cervicothoracic region
M45.4	Ankylosing spondylitis of thoracic region
M45.5	Ankylosing spondylitis of thoracolumbar region
M45.6	Ankylosing spondylitis lumbar region

ICD-10 Code	Description
M45.7	Ankylosing spondylitis of lumbosacral region
M45.8	Ankylosing spondylitis sacral and sacrococcygeal region
M45.9	Ankylosing spondylitis of unspecified sites in spine
M48.8X1	Other specified spondylopathies, occipito-atlanto-axial region
M48.8X2	Other specified spondylopathies, cervical region
M48.8X3	Other specified spondylopathies, cervicothoracic region
M48.8X4	Other specified spondylopathies, thoracic region
M48.8X5	Other specified spondylopathies, thoracolumbar region
M48.8X6	Other specified spondylopathies, lumbar region
M48.8X7	Other specified spondylopathies, lumbosacral region
M48.8X8	Other specified spondylopathies, sacral and sacrococcygeal region
M48.8X9	Other specified spondylopathies, site unspecified

Background

Infliximab is a genetically engineered chimeric monoclonal antibody against tumor necrosis factor alfa (TNF-alfa), which is a key mediator of mucosal inflammation. Increased levels of TNF-alfa are found in the intestinal mucosa and stool of patients with active Crohn's disease and in the joints of rheumatoid arthritis patients. Elevated TNF-alfa concentrations are also involved in ulcerative colitis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis. Remicade, an intravenously (IV)-administered tumor necrosis factor (TNF) inhibitor, was FDA-approved in 1998 for the treatment of Crohn's disease (CD) and has since gained 7 additional indications (*Remicade package insert 2025*). There are now 3 FDA-approved intravenous biosimilars for Remicade; Inflectra (infliximab-dyyb) Renflexis (infliximab-abda), and Avsola (infliximab-axxq) and 1 subcutaneous formulation, Zymfentra (infliximab-dyyb).

Clinical Evidence

Rheumatoid Arthritis

The safety and efficacy of Infliximab in adult patients with RA were assessed in 2 multicenter, randomized, double-blind, pivotal trials: ATTRACT (Study RA I) and ASPIRE (Study RA II) (*Remicade package insert 2025*). Concomitant use of stable doses of folic acid, oral corticosteroids (≤10 mg/day) and/or non-steroidal anti-inflammatory drugs (NSAIDs) was permitted. Study RA I was a placebo-controlled study of 428 patients with active RA despite treatment with methotrexate (MTX). Patients enrolled had a median age of 54 years, median disease duration of 8.4 years, median swollen and tender joint count of 20 and 31 respectively and were on a median dose of 15 mg/wk of MTX. Patients received either placebo+MTX or one of 4 doses/schedules of Infliximab+MTX: 3 mg/kg or 10 mg/kg of Infliximab by IV infusion at Weeks 0, 2 and 6 followed by additional infusions every 4 or 8 weeks in combination with MTX. In Study RA I, all doses/schedules of Infliximab+MTX resulted in improvement in signs and symptoms as measured by the American College of Rheumatology response criteria (ACR 20) with a higher percentage of patients achieving an ACR 20, 50 and 70 compared to placebo+MTX. This improvement was observed at Week 2 and maintained through week 102. Greater effects on each component of the ACR 20 were observed in all patients 38 treated with Infliximab+MTX compared to placebo+MTX. More patients treated with Infliximab reached a major clinical response than placebo-treated patients. Structural damage in both hands and feet was assessed radiographically at Week 54 by the change from baseline in the van der Heijde-modified Sharp (vdH-S) score, a composite score 39 of structural damage that measures the number and size of joint erosions and the degree of joint space narrowing in hands/wrists and feet. In Study RA I, approximately 80% of patients had paired X-ray data at 54 weeks and approximately 70% at 102 weeks. The inhibition of progression of structural damage was observed at 54 weeks and maintained through 102 weeks. Physical function and disability were

assessed using the Health Assessment Questionnaire (HAQ-DI) and the general health-related quality of life questionnaire SF-36. In Study RA I, all doses/schedules of Infliximab+MTX showed significantly greater improvement from baseline in HAQ-DI and SF-36 physical component summary score averaged over time through Week 54 compared to placebo+MTX, and no worsening in the SF-36 mental component summary score. The median (interquartile range) improvement from baseline to Week 54 in HAQ-DI was 0.1 (-0.1, 0.5) for the placebo+MTX group and 0.4 (0.1, 0.9) for Infliximab+MTX ($p<0.001$). Both HAQ-DI and SF-36 effects were maintained through Week 102. Approximately 80% of patients in all doses/schedules of Infliximab+MTX remained in the trial through 102 weeks.

Study RA II was a placebo-controlled study of 3 active treatment arms in 1004 MTX naive patients of 3 or fewer years' duration active RA. Patients enrolled had a median age of 51 years with a median disease duration of 0.6 years, median swollen and tender joint count of 19 and 31, respectively, and >80% of patients had baseline joint erosions. At randomization, all patients received MTX (optimized to 20 mg/wk by Week 8) and either placebo, 3 mg/kg or 6 mg/kg Infliximab at Weeks 0, 2, and 6 and every 8 weeks thereafter. Data on use of Infliximab without concurrent MTX are limited. In Study RA II, after 54 weeks of treatment, both doses of Infliximab+MTX resulted in statistically significantly greater response in signs and symptoms compared to MTX alone as measured by the proportion of patients achieving ACR 20, 50 and 70 responses. More patients treated with Infliximab reached a major clinical response than placebo-treated patients. In Study RA II, >90% of patients had at least 2 evaluable X-rays. Inhibition of progression of structural damage was observed at Weeks 30 and 54 in the Infliximab+MTX groups compared to MTX alone. Patients treated with Infliximab+MTX demonstrated less progression of structural damage compared to MTX alone, whether baseline acute-phase reactants (ESR and CRP) were normal or elevated: patients with elevated baseline acute phase reactants treated with MTX alone demonstrated a mean progression in vdH-S score of 4.2 units compared to patients treated with Infliximab+MTX who demonstrated 0.5 units of progression; patients with normal baseline acute phase reactants treated with MTX alone demonstrated a mean progression in vdH-S score of 1.8 units compared to Infliximab+MTX who demonstrated 0.2 units of progression. Of patients receiving Infliximab+MTX, 59% had no progression (vdH-S score ≤0 unit) of structural damage compared to 45% of patients receiving MTX alone. In a subset of patients who began the study without erosions, Infliximab+MTX maintained an erosion-free state at 1 year in a greater proportion of patients than MTX alone, 79% (77/98) vs. 58% (23/40), respectively ($P<0.01$). Fewer patients in the Infliximab+MTX groups (47%) developed erosions in uninvolved joints compared to MTX alone (59%). In Study RA II, both Infliximab treatment groups showed greater improvement in HAQ-DI from baseline averaged over time through Week 54 compared to MTX alone; 0.7 for Infliximab+MTX vs. 0.6 for MTX alone ($P\leq0.001$). No worsening in the SF-36 mental component summary score was observed.

Psoriatic Arthritis

Safety and efficacy of Infliximab were assessed in a multicenter, double-blind, placebo-controlled study in 200 adult patients with active PsA despite disease-modifying antirheumatic drug (DMARD) or NSAID therapy (≥5 swollen joints and ≥5 tender joints) with 1 or more of the following subtypes: arthritis involving DIP joints (n=49), arthritis mutilans (n=3), asymmetric peripheral arthritis (n=40), polyarticular arthritis (n=100), and spondylitis with peripheral arthritis (n=8) (*Remicade package insert 2025*) . Patients also had Ps with a qualifying target lesion ≥2 cm in diameter. Forty-six percent of patients continued on stable doses of methotrexate (≤25 mg/week). During the 24-week double-blind phase, patients received either 5 mg/kg Infliximab or placebo at Weeks 0, 2, 6, 14, and 22 (100 patients in each group). At Week 16, placebo patients with <10% improvement from baseline in both swollen and tender joint counts were switched to Infliximab induction (early escape). At Week 24, all placebo-treated patients crossed over to Infliximab induction. Dosing continued for all patients through Week 46.

Treatment with Infliximab resulted in improvement in signs and symptoms, as assessed by the ACR criteria, with 58% of Infliximab-treated patients achieving ACR 20 at Week 14, compared with 11% of placebo-treated patients ($P<0.001$). The response was similar regardless of concomitant use of methotrexate. Improvement was observed as early as Week 2. At 6 months, the ACR 20/50/70 responses were achieved by 54%, 41%, and 27%, respectively, of patients receiving Infliximab compared to 16%, 4%, and 2%, respectively, of patients receiving placebo. Similar responses were seen in patients with each of the subtypes of PsA, although few patients were enrolled with the arthritis mutilans and

spondylitis with peripheral arthritis subtypes. Compared to placebo, treatment with Infliximab resulted in improvements in the components of the ACR response criteria, as well as in dactylitis and enthesopathy. The clinical response was maintained through Week 54. Similar ACR responses were observed in an earlier randomized, placebo-controlled study of 104 PsA patients, and the responses were maintained through 98 weeks in an open-label extension phase.

Improvement in Psoriasis Area and Severity Index (PASI) in PsA patients with baseline body surface area (BSA) ≥3% (n=87 placebo, n=83 Infliximab) was achieved at Week 14, regardless of concomitant methotrexate use, with 64% of Infliximab-treated patients achieving at least 75% improvement from baseline vs. 2% of placebo-treated patients; improvement was observed in some patients as early as Week 2. At 6 months, the PASI 75 and PASI 90 responses were achieved by 60% and 39%, respectively, of patients receiving Infliximab compared to 1% and 0%, respectively, of patients receiving placebo. The PASI response was generally maintained through Week 54.

Structural damage in both hands and feet was assessed radiographically by the change from baseline in the van der Heijde-Sharp (vdH-S) score, modified by the addition of hand DIP joints. The total modified vdH-S score is a composite score of structural damage that measures the number and size of joint erosions and the degree of joint space narrowing (JSN) in the hands and feet. At Week 24, Infliximab-treated patients had less radiographic progression than placebo-treated patients (mean change of -0.70 vs. 0.82, P<0.001). Infliximab-treated patients also had less progression in their erosion scores (-0.56 vs 0.51) and JSN scores (-0.14 vs 0.31). The patients in the Infliximab group demonstrated continued inhibition of structural damage at Week 54. Most patients showed little or no change in the vdH-S score during this 12-month study (median change of 0 in both patients who initially received Infliximab or placebo). More patients in the placebo group (12%) had readily apparent radiographic progression compared with the Infliximab group (3%).

Physical function status was assessed using the HAQ Disability Index (HAQ-DI) and the SF36 Health Survey. Infliximab-treated patients demonstrated significant improvement in physical function as assessed by HAQ-DI (median percent improvement in HAQ-DI score from baseline to Week 14 and 24 of 43% for Infliximab-treated patients vs 0% for placebotreated patients). During the placebo-controlled portion of the trial (24 weeks), 54% of Infliximab-treated patients achieved a clinically meaningful improvement in HAQ-DI (≥0.3 unit decrease) compared to 22% of placebo-treated patients. Infliximab-treated patients also demonstrated greater improvement in the SF-36 physical and mental component summary scores than placebo-treated patients. The responses were maintained for up to 2 years in an open-label extension study.

Plaque Psoriasis

The safety and efficacy of Infliximab were assessed in 3 randomized, double-blind, placebo-controlled studies in patients 18 years of age and older with chronic, stable Ps involving ≥10% BSA, a minimum PASI score of 12, and who were candidates for systemic therapy or phototherapy (*Remicade package insert 2025*). Patients with guttate, pustular, or erythrodermic psoriasis were excluded from these studies. No concomitant anti-psoriatic therapies were allowed during the study, with the exception of low-potency topical corticosteroids on the face and groin after Week 10 of study initiation. Study I (EXPRESS) evaluated 378 patients who received placebo or Infliximab at a dose of 5 mg/kg at Weeks 0, 2, and 6 (induction therapy), followed by maintenance therapy every 8 weeks. At Week 24, the placebo group crossed over to Infliximab induction therapy (5 mg/kg), followed by maintenance therapy every 8 weeks. Patients originally randomized to Infliximab continued to receive Infliximab 5 mg/kg every 8 weeks through Week 46. Across all treatment groups, the median baseline PASI score was 21 and the baseline Static Physician Global Assessment (sPGA) score ranged from moderate (52% of patients) to marked (36%) to severe (2%). In addition, 75% of patients had a BSA >20%. Seventy-one percent of patients previously received systemic therapy, and 82% received phototherapy. Study II (EXPRESS II) evaluated 835 patients who received placebo or Infliximab at doses of 3 mg/kg or 5 mg/kg at Weeks 0, 2, and 6 (induction therapy). At Week 14, within each Infliximab dose group, patients were randomized to either scheduled (every 8 weeks) or as needed (PRN) maintenance treatment through Week 46. At Week 16, the placebo group crossed over to Infliximab induction therapy (5 mg/kg), followed by maintenance therapy every 8 weeks. Across all treatment groups, the median baseline PASI score was 18, and 63% of patients had a BSA >20%. Fifty-five percent of

patients previously received systemic therapy, and 64% received phototherapy. Study III (SPIRIT) evaluated 249 patients who had previously received either psoralen plus ultraviolet A treatment (PUVA) or other systemic therapy for their psoriasis. These patients were randomized to receive either placebo or Infliximab at doses of 3 mg/kg or 5 mg/kg at Weeks 0, 2, and 6. At Week 26, patients with a sPGA score of moderate or worse (greater than or equal to 3 on a scale of 0 to 5) received an additional dose of the randomized treatment. Across all treatment groups, the median baseline PASI score was 19, and the baseline sPGA score ranged from moderate (62% of patients) to marked (22%) to severe (3%). In addition, 75% of patients had a BSA >20%. Of the enrolled patients, 114 (46%) received the Week 26 additional dose.

In Studies I, II and III, the primary endpoint was the proportion of patients who achieved a reduction in score of at least 75% from baseline at Week 10 by the PASI (PASI 75). In Study I and Study III, another evaluated outcome included the proportion of patients who achieved a score of "cleared" or "minimal" by the sPGA. The sPGA is a 6-category scale ranging from "5 = severe" to "0 = cleared" indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema, and scaling. Treatment success, defined as "cleared" or "minimal," consisted of none or minimal elevation in plaque, up to faint red coloration in erythema, and none or minimal fine scale over <5% of the plaque. Study II also evaluated the proportion of patients who achieved a score of "clear" or "excellent" by the relative Physician's Global Assessment (rPGA). The rPGA is a 6-category scale ranging from "6 = worse" to "1 = clear" that was assessed relative to baseline. Overall induration, scaling, and erythema. Treatment success, defined as "clear" or "excellent," consisted of some residual pinkness or pigmentation to marked improvement (nearly normal skin texture; some erythema may be present).

In Study I, in the subgroup of patients with more extensive Ps who had previously received phototherapy, 85% of patients on 5 mg/kg Infliximab achieved a PASI 75 at Week 10 compared with 4% of patients on placebo. In Study II, in the subgroup of patients with more extensive Ps who had previously received phototherapy, 72% and 77% of patients on 3 mg/kg and 5 mg/kg Infliximab achieved a PASI 75 at Week 10 respectively compared with 1% on placebo. In Study II, among patients with more extensive Ps who had failed or were intolerant to phototherapy, 70% and 78% of patients on 3 mg/kg and 5 mg/kg Infliximab achieved a PASI 75 at Week 10 respectively, compared with 2% on placebo. Maintenance of response was studied in a subset of 292 and 297 Infliximab-treated patients in the 3 mg/kg and 5 mg/kg groups: respectively, in Study II. Stratified by PASI response at Week 10 and investigational site, patients in the active treatment groups were re-randomized to either a scheduled or as needed maintenance (PRN) therapy, beginning on Week 14. The groups that received a maintenance dose every 8 weeks appear to have a greater percentage of patients maintaining a PASI 75 through Week 50 as compared to patients who received the as-needed or PRN doses, and the best response was maintained with the 5 mg/kg every 8-week dose. At Week 46, when Infliximab serum concentrations were at trough level, in the every 8-week dose group, 54% of patients in the 5 mg/kg group compared to 36% in the 3 mg/kg group achieved PASI 75. The lower percentage of PASI 75 responders in the 3 mg/kg every 8-week dose group compared to the 5 mg/kg group was associated with a lower percentage of patients with detectable trough serum infliximab levels. This may be related in part to higher antibody. In addition, in a subset of patients who had achieved a response at Week 10, maintenance of response appears to be greater in patients who received Infliximab every 8 weeks at the 5 mg/kg dose. Regardless of whether the maintenance doses are PRN or every 8 weeks, there is a decline in response in a subpopulation of patients in each group over time. The results of Study I through Week 50 in the 5 mg/kg every 8 weeks maintenance dose group were similar to the results from Study II. Efficacy and safety of Infliximab treatment beyond 50 weeks have not been evaluated in patients with Ps.

Ankylosing Spondylitis

The safety and efficacy of Infliximab were assessed in a randomized, multicenter, double-blind, placebo-controlled study in 279 adult patients with active AS (*Remicade package insert 2025*). Patients were between 18 and 74 years of age, and had AS, as defined by the modified New York criteria for Ankylosing Spondylitis. Patients were to have had active disease as evidenced by both a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score >4 (possible range 0-10) and spinal pain >4 (on a Visual Analog Scale [VAS] of 0-10). Patients with complete ankylosis of the spine were excluded from study participation, and the use of Disease Modifying Anti-Rheumatic Drugs (DMARDs) and systemic corticosteroids were prohibited. Doses of Infliximab 5 mg/kg or placebo were administered intravenously at Weeks 0, 2, 6, 12 and 18. At

24 weeks, improvement in the signs and symptoms of AS, as measured by the proportion of patients achieving a 20% improvement in ASAS response criteria (ASAS 20), was seen in 60% of patients in the Infliximab-treated group vs. 18% of patients in the placebo group (p<0.001). Improvement was observed at Week 2 and maintained through Week 24.

At 24 weeks, the proportions of patients achieving a 50% and a 70% improvement in the signs and symptoms of AS, as measured by ASAS response criteria (ASAS 50 and ASAS 70, respectively), were 44% and 28%, respectively, for patients receiving Infliximab, compared to 9% and 4%, respectively, for patients receiving placebo (P<0.001, Infliximab vs. placebo). A low level of disease activity (defined as a value <20 [on a scale of 0-100 mm] in each of the 4 ASAS response parameters) was achieved in 22% of Infliximab-treated patients vs. 1% in placebo-treated patients (P<0.001).

The median improvement from baseline in the general health-related quality-of-life questionnaire SF-36 physical component summary score at Week 24 was 10.2 for the Infliximab group vs. 0.8 for the placebo group (P<0.001). There was no change in the SF-36 mental component summary score in either the Infliximab group or the placebo group. Results of this study were similar to those seen in a multicenter double-blind, placebo controlled study of 70 patients with AS.

Crohn's Disease
The safety and efficacy of single and multiple doses of Infliximab were assessed in 2 randomized, double-blind, placebo-controlled clinical studies in 653 adult patients with moderate to severely active CD [Crohn's Disease Activity Index (CDAI) ≥220 and ≤400] with an inadequate response to prior conventional therapies (*Remicade package insert 2025*). Concomitant stable doses of aminosalicylates, corticosteroids and/or immunomodulatory agents were permitted and 92% of patients continued to receive at least one of these medications. In the single-dose trial of 108 adult patients, 16% (4/25) of placebo patients achieved a clinical response (decrease in CDAI ≥70 points) at Week 4 vs. 81% (22/27) of patients receiving 5 mg/kg Infliximab (p<0.001, two-sided, Fisher's Exact test). Additionally, 4% (1/25) of placebo patients and 48% (13/27) of patients receiving 5 mg/kg Infliximab achieved clinical remission (CDAI<150) at Week 4. In a multidose trial (ACCENT I [Study Crohn's I]), 545 adult patients received 5 mg/kg at Week 0 and were then randomized to one of three treatment groups; the placebo maintenance group received placebo at Weeks 2 and 6, and then every 8 weeks; the 5 mg/kg maintenance group received 5 mg/kg at Weeks 2 and 6, and then every 8 weeks; and the 10 mg/kg maintenance group received 5 mg/kg at Weeks 2 and 6, and then 10 mg/kg every 8 weeks. Patients in response at Week 2 were randomized and analyzed separately from those not in response at Week 2. Corticosteroid taper was permitted after Week 6. At Week 2, 57% (311/545) of patients were in clinical response. At Week 30, a significantly greater proportion of these patients in the 5 mg/kg and 10 mg/kg maintenance groups achieved clinical remission compared to patients in the placebo maintenance group. Additionally, a significantly greater proportion of patients in the 5 mg/kg and 10 mg/kg Infliximab maintenance groups were in clinical remission and were able to discontinue corticosteroid use compared to patients in the placebo maintenance group at Week 54.

Patients in the Infliximab maintenance groups (5 mg/kg and 10 mg/kg) had a longer time to loss of response than patients in the placebo maintenance group. At Weeks 30 and 54, significant improvement from baseline was seen among the 5 mg/kg and 10 mg/kg Infliximab-treated groups compared to the placebo group in the disease-specific inflammatory bowel disease questionnaire (IBDQ), particularly the bowel and systemic components, and in the physical component summary score of the general health-related quality of life questionnaire SF-36.

In a subset of 78 patients who had mucosal ulceration at baseline and who participated in an endoscopic sub study, 13 of 43 patients in the Infliximab maintenance group had endoscopic evidence of mucosal healing compared to 1 of 28 patients in the placebo group at Week 10. Of the Infliximab-treated patients showing mucosal healing at Week 10, 9 of 12 patients also showed mucosal healing at Week 54. Patients who achieved a response and subsequently lost response were eligible to receive Infliximab on an episodic basis at a dose that was 5 mg/kg higher than the dose to which they were randomized. The majority of such patients responded to the higher dose. Among patients who were not in response at Week 2, 59% (92/157) of Infliximab maintenance patients responded by Week 14 compared to 51% (39/77) of placebo maintenance patients. Among patients who did not respond by Week 14, additional therapy did not result in

significantly more responses.

The safety and efficacy of Infliximab were assessed in 2 randomized, double-blind, placebo-controlled studies in adult patients with fistulizing CD with fistula(s) that were of at least 3 months duration. Concomitant use of stable doses of corticosteroids, 5-aminosalicylates, antibiotics, MTX, 6-mercaptopurine (6-MP) and/or azathioprine (AZA) was permitted. In the first trial, 94 adult patients received 3 doses of either placebo or Infliximab at Weeks 0, 2 and 6. Fistula response (≥50% reduction in number of enterocutaneous fistulas draining upon gentle compression on at least 2 consecutive visits without an increase in medication or surgery for CD) was seen in 68% (21/31) of patients in the 5 mg/kg Infliximab group (P=0.002) and 56% (18/32) of patients in the 10 mg/kg Infliximab group (P=0.021) vs. 26% (8/31) of patients in the placebo arm. The median time to onset of response and median duration of response in Infliximab-treated patients was 2 and 12 weeks, respectively. Closure of all fistulas was achieved in 52% of Infliximab-treated patients compared with 13% of placebo-treated patients (P<0.001). In the second trial (ACCENT II [Study Crohn's II]), adult patients who were enrolled had to have at least 1 draining enterocutaneous (perianal, abdominal) fistula. All patients received 5 mg/kg Infliximab at Weeks 0, 2 and 6. Patients were randomized to placebo or 5 mg/kg Infliximab maintenance at Week 14. Patients received maintenance doses at Week 14 and then every 8 weeks through Week 46. Patients who were in fistula response (fistula response was defined the same as in the first trial) at both Weeks 10 and 14 were randomized separately from those not in response. The primary endpoint was time from randomization to loss of response among those patients who were in fistula response. Among the randomized patients (273 of the 296 initially enrolled), 87% had perianal fistulas and 14% had abdominal fistulas. Eight percent also had rectovaginal fistulas. Greater than 90% of the patients had received previous immunosuppressive and antibiotic therapy. At Week 14, 65% (177/273) of patients were in fistula response. Patients randomized to Infliximab maintenance had a longer time to loss of fistula response compared to the placebo maintenance group. At Week 54, 38% (33/87) of Infliximab-treated patients had no draining fistulas compared with 22% (20/90) of placebo-treated patients (P=0.02). Compared to placebo maintenance, patients on Infliximab maintenance had a trend toward fewer hospitalizations. Patients who achieved a fistula response and subsequently lost response were eligible to receive Infliximab maintenance therapy at a dose that was 5 mg/kg higher than the dose to which they were randomized. Of the placebo maintenance patients, 66% (25/38) responded to 5 mg/kg Infliximab, and 57% (12/21) of Infliximab maintenance patients responded to 10 mg/kg. Patients who had not achieved a response by Week 14 were unlikely to respond to additional doses of Infliximab. Similar proportions of patients in either group developed new fistulas (17% overall) and similar numbers developed abscesses (15% overall).

The safety and efficacy of Infliximab in pediatric patients were assessed in a randomized, open-label study (Study Peds Crohn's) in 112 pediatric patients aged 6 to 17 years old with moderately to severely active CD and an inadequate response to conventional therapies. The median age was 13 years, and the median Pediatric Crohn's Disease Activity Index (PCDAI) was 40 (on a scale of 0 to 100). All patients were required to be on a stable dose of 6-MP, AZA, or MTX; 35% were also receiving corticosteroids at baseline. All patients received induction dosing of 5 mg/kg Infliximab at Weeks 0, 2, and 6. At Week 10, 103 patients were randomized to a maintenance regimen of 5 mg/kg Infliximab given either every 8 weeks or every 12 weeks. At Week 10, 88% of patients were in clinical response (defined as a decrease from baseline in the PCDAI score of ≥15 points and total PCDAI score of ≤30 points), and 59% were in clinical remission (defined as PCDAI score of ≤10 points). The proportion of pediatric patients achieving clinical response at Week 10 compared favorably with the proportion of adults achieving a clinical response in Study Crohn's I. The study definition of clinical response in Study Peds Crohn's was based on the PCDAI score, whereas the CDAI score was used in the adult Study Crohn's I. At both Week 30 and Week 54, the proportion of patients in clinical response was greater in the every 8-week treatment group than in the every 12-week treatment group (73% vs. 47% at Week 30, and 64% vs. 33% at Week 54). At both Week 30 and Week 54, the proportion of patients in clinical remission was also greater in the every 8-week treatment group than in the every 12-week treatment group (60% vs. 35% at Week 30, and 56% vs. 24% at Week 54). For patients in Study Peds Crohn's receiving corticosteroids at baseline, the proportion of patients able to discontinue corticosteroids while in remission at Week 30 was 46% for the every 8-week maintenance group and 33% for the every 12-week maintenance group. At Week 54, the proportion of patients able to discontinue corticosteroids while in remission was 46% for the every 8-week maintenance group and 17% for the every 12-week maintenance group.

The safety and efficacy of Zymfentra (infliximab) SC injection were assessed in a Phase 3 randomized, double-blind, placebo-controlled study in adult subjects with moderately to severely active CD (LIBERTY-CD). All patients received three IV induction doses at weeks 0, 2 and 6. In order to be randomized to treatment in the study, patients had to be in clinical response at week 10. A total of 323 patients were randomized at week 10 to Zymfentra or placebo every 2 weeks. The co-primary endpoints were clinical remission (based on Crohn's Disease Activity Index [CDAI]) and endoscopic response at week 54. Clinical remission was achieved in 63% and 30% of patients treated with Zymfentra and placebo, respectively (treatment difference 35, 95% CI: 24, 45; $p < 0.0001$). Endoscopic response was achieved in 50% and 18% of patients treated with Zymfentra and placebo, respectively (treatment difference 34, 95% CI: 23, 43; $p < 0.0001$).

Ulcerative Colitis

The safety and efficacy of Infliximab were assessed in 2 randomized, double-blind, placebo controlled clinical studies in 728 adult patients with moderately to severely active UC (Mayo score 6 to 12 [of possible range 0 to 12], Endoscopy sub score ≥2) with an inadequate response to conventional oral therapies (Studies UC I and UC II) (*Remicade package insert 2025*). Concomitant treatment with stable doses of aminosalicylates, corticosteroids and/or immunomodulatory agents was permitted. Corticosteroid taper was permitted after Week 8. Patients were randomized at week 0 to receive either placebo, 5 mg/kg Infliximab or 10 mg/kg Infliximab at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 46 in Study UC I, and at Weeks 0, 2, 6, and every 8 weeks thereafter through Week 22 in Study UC II. In Study UC II, patients were allowed to continue blinded therapy to Week 46 at the investigator's discretion. Adult patients in Study UC I had failed to respond or were intolerant to oral corticosteroids, 6-MP, or AZA. Adult patients in Study UC II had failed to respond or were intolerant to the above treatments and/or aminosalicylates. Similar proportions of patients in Studies UC I and UC II were receiving corticosteroids (61% and 51%, respectively), 6-MP/AZA (49% and 43%) and aminosalicylates (70% and 75%) at baseline. More patients in Study UC II than UC I were taking solely aminosalicylates for UC (26% vs. 11%, respectively). Clinical response was defined as a decrease from baseline in the Mayo score by ≥30% and ≥3 points, accompanied by a decrease in the rectal bleeding subscore of ≥1 or a rectal bleeding subscore of 0 or 1.

In both Study UC I and Study UC II, greater percentages of patients in both Infliximab groups achieved clinical response, clinical remission, and mucosal healing than in the placebo group. Each of these effects was maintained through the end of each trial (Week 54 in Study UC I, and Week 30 in Study UC II). In addition, a greater proportion of patients in Infliximab groups demonstrated sustained response and sustained remission than in the placebo groups. Of patients on corticosteroids at baseline, greater proportions of adult patients in the Infliximab treatment groups were in clinical remission and able to discontinue corticosteroids at Week 30 compared with the patients in the placebo treatment groups (22% in Infliximab treatment groups vs. 10% in placebo group in Study UC I; 23% in Infliximab treatment groups vs. 3% in placebo group in Study UC II). In Study UC I, this effect was maintained through Week 54 (21% in Infliximab treatment groups vs. 9% in placebo group). The Infliximab-associated response was generally similar in the 5 mg/kg and 10 mg/kg dose groups. The improvement with Infliximab was consistent across all Mayo sub scores through Week 54.

The safety and effectiveness of Infliximab for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients aged 6 years and older with moderately to severely active UC who have had an inadequate response to conventional therapy are supported by evidence from adequate and well-controlled studies of Infliximab in adults. Additional safety and pharmacokinetic data were collected in an open-label pediatric UC trial in 60 pediatric patients aged 6 through 17 years (median age 14.5 years) with moderately to severely active UC (Mayo score of 6 to 12; Endoscopic subscore ≥2) and an inadequate response to conventional therapies. At baseline, the median Mayo score was 8, 53% of patients were receiving immunomodulator therapy (6-MP/AZA/MTX), and 62% of patients were receiving corticosteroids (median dose 0.5 mg/kg/day in prednisone equivalents). Discontinuation of immunomodulators and corticosteroid taper were permitted after Week 0. All patients received induction dosing of 5 mg/kg Infliximab at Weeks 0, 2, and 6. Patients who did not respond to Infliximab at Week 8 received no further Infliximab and returned for safety follow-up. At Week 8, 45 patients were randomized to a maintenance regimen of 5 mg/kg Infliximab given either every 8 weeks through Week 46 or every 12 weeks through Week 42. Patients were

allowed to change to a higher dose and/or more frequent administration schedule if they experienced loss of response. Clinical response at Week 8 was defined as a decrease from baseline in the Mayo score by ≥30% and ≥3 points, including a decrease in the rectal bleeding subscore by ≥1 points or achievement of a rectal bleeding subscore of 0 or 1. Clinical remission at Week 8 was measured by the Mayo score, defined as a Mayo score of ≤2 points with no individual subscore >1. Clinical remission was also assessed at Week 8 and Week 54 using the Pediatric Ulcerative Colitis Activity Index (PUCAI)1 score and was defined by a PUCAI score of <10 points. Endoscopies were performed at baseline and at Week 8. A Mayo endoscopy subscore of 0 indicated normal or inactive disease and a subscore of 1 indicated mild disease (erythema, decreased vascular pattern, or mild friability). Of the 60 patients treated, 44 were in clinical response at Week 8. Of 32 patients taking concomitant immunomodulators at baseline, 23 achieved clinical response at Week 8, compared to 21 of 28 of those not taking concurrent immunomodulators at baseline. At Week 8, 24 of 60 patients were in clinical remission as measured by the Mayo score and 17 of 51 patients were in remission as measured by the PUCAI score. At Week 54, 8 of 21 patients in the every 8-week maintenance group and 4 of 22 patients in the every 12-week maintenance group achieved remission as measured by the PUCAI score. During maintenance phase, 23 of 45 randomized patients (9 in the every 8-week group and 14 in the every 12-week group) required an increase in their dose and/or increase in frequency of Infliximab administration due to loss of response. Nine of the 23 patients who required a change in dose had achieved remission at Week 54. Seven of those patients received the 10 mg/kg every 8-week dosing.

The safety and efficacy of Zymfentra (infliximab) SC injection were assessed in a Phase 3 randomized, double-blind, placebo-controlled study (LIBERY-UC) in adult patients with moderately to severely active UC. All patients received three IV induction doses at weeks 0, 2 and 6. In order to be randomized to treatment in the study, patients had to be in clinical response at week 10. A total of 438 patients were randomized at week 10 to Zymfentra or placebo every 2 weeks. The primary endpoint was the proportion of patients in clinical remission at week 54. Clinical remission was achieved in 43% and 21% of patients treated with Zymfentra and placebo, respectively (treatment difference 21, 95% CI: 12, 29; $p < 0.0001$).

Sarcoidosis
The use of infliximab in patients with chronic pulmonary sarcoidosis was assessed in a multicenter, randomized, double-blind, placebo-controlled study *(Baughman et al 2006*). Patients must have been treated with at least 10 mg/d of prednisone or equivalent or one or more immunosuppressants for ≥ 3 months before screening. They received infliximab 3 mg/kg (n = 46), 5 mg/kg (n = 47), or placebo (n = 45) at weeks 0, 2, 6, 12, 18, and 24. They were followed through 52 weeks. The primary endpoint was the change at week 24 from baseline in percent of predicted forced vital capacity (FVC). Patients receiving infliximab 3 or 5 mg/kg had a mean increase of 2.5% compared with no change for those receiving placebo ($p = 0.038$).

Clinical Guidelines

Rheumatoid Arthritis
The 2021 guidelines from American College of Rheumatology (ACR) state that despite low-certainty evidence supporting greater improvement in disease activity with methotrexate plus a TNF inhibitor, methotrexate monotherapy is preferred over the combination because many patients will reach their goal on methotrexate monotherapy and because of the additional risks of toxicity and higher costs associated with TNF inhibitors (*Fraenkel et al 2021*). This recommendation is conditional because some patients, particularly those with poor prognostic factors, may prioritize more rapid onset of action and greater chance of improvement associated with combination therapy over the additional risks and costs associated with initial use of methotrexate in combination with a TNF inhibitor.

Psoriatic Arthritis
The 2018 guidelines from ACR (2018) recommend a TNF inhibitor biologic agent over an oral small molecule (OSM) as a first-line option in treatment-naive patients with active PsA (*Singh et al 2018*). OSMs may be used instead of a TNF inhibitor biologic in patients without severe PsA and without severe psoriasis (final determination of severity to be made by the patient and the health care provider), those who prefer an oral drug instead of parenteral therapy, or those with

contraindications to TNF inhibitor treatment, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease. All recommendations for treatment-naive patients with active PsA are conditional based on low- to very-low-quality evidence. For treatment-naive patients with active PsA, the use of a TNF inhibitor biologic or OSM is recommended over an interleukin-17 inhibitor (IL-17i) or IL-12/23i biologic. An IL-17i or IL-12/23i biologic may be used instead of TNF inhibitor biologics in patients with severe psoriasis or contraindications to TNF inhibitor biologics and may be used instead of OSMs in patients with severe psoriasis or severe PsA.

Plaque Psoriasis
Guidelines from the American Academy of Dermatologists (AAD) and National Psoriasis Foundation (NPF) recommend infliximab as a monotherapy treatment option for adults with moderate to severe plaque psoriasis (*Menter et al 2019*).

Ankylosing Spondylitis
Updated guidelines for ankylosing spondylitis and non-radiographic axial spondyloarthritis are published by the American College of Rheumatology (ACR)/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (*Ward et al 2019*). The guidelines strongly recommend treatment with TNF inhibitor over no treatment with TNF inhibitor, in adults with active AS despite treatment with NSAIDs. In In adults with active AS despite treatment with the first TNF inhibitor used, they conditionally recommend treatment with secukinumab or ixekizumab over treatment with a different TNF inhibitor in patients with primary non-response to TNF inhibitor. In adults with active AS despite treatment with the first TNF inhibitor used, they conditionally recommend treatment with a different TNF inhibitor over treatment with a non-TNF inhibitor biologic in patients with secondary non-response to TNF inhibitor. In adults with active AS despite treatment with the first TNF inhibitor used, they strongly recommend against switching to treatment with a biosimilar of the first TNF inhibitor.

Crohn's Disease
The American College of Gastroenterology (ACG) guideline for Crohn's disease listed TNF inhibitors as an option for disease that is resistant to corticosteroids, severely active disease, perianal fistulizing disease, and maintenance of remission (*Lichtenstein et al 2018*). The guideline made a conditional recommendation that in high-risk patients, anti-TNF agents should be started within 4 weeks of surgery in order to prevent postoperative Crohn's disease recurrence. Guidelines from the American Gastroenterological Association (AGA) include infliximab among the therapies for moderate to severe Crohn's disease, for induction and maintenance of remission (*Feuerstein et al 2021*).

The 2024 ECCO guideline on medical treatment in CD recommends the use of infliximab, adalimumab, ustekinumab, risankizumab, vedolizumab, and upadacitinib to induce remission and maintenance of remission in patients with moderate-to-severe CD (*Gordon et al 2024*). Other immunomodulator-related recommendations within the guideline include:

- Recommending combination therapy with infliximab and thiopurines when starting infliximab as induction therapy in patients with moderate-to-severe CD and recommending combination therapy for a minimum of 6 to 12 months.
- Suggesting against the combination of adalimumab and thiopurines over adalimumab alone to achieve clinical remission and response.
- Suggesting certolizumab can be used as induction therapy and maintenance therapy in moderate-to-severe CD.
- Suggesting adalimumab or ustekinumab are equally effective as induction and maintenance therapy in biologic-naïve patients with moderate-to-severe CD.

Ulcerative Colitis
The American College of Gastroenterology (ACG) guideline for ulcerative colitis notes that the following agents can be used for induction of remission in moderately to severely active disease: budesonide extended-release tablets; oral or intravenous systemic corticosteroids, Entyvio® (vedolizumab intravenous infusion), Xeljanz®/XR (tofacitinib tablets/extended-release tablets), or TNF inhibitor therapy (*Rubin et al 2019*). For adult outpatients with moderate to

severe UC, a 2020 AGA guideline strongly recommends using infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab over no treatment (*Feuerstein et al 2020*).

For adult outpatients with moderate to severe UC, an American Gastroenterological Association (AGA) living guideline was last updated in 2024, and recommends using infliximab, golimumab, vedolizumab, tofacitinib, upadacitinib, ustekinumab, ozanimod, etrasimod, risankizumab, and guselkumab over no treatment and suggests use of adalimumab, filgotinib (not approved in the U.S.) or mirikizumab over no treatment (*Singh et al 2024*). Biosimilars of infliximab, adalimumab, and ustekinumab are considered equivalent to the reference drug. Subcutaneous formulations of infliximab and vedolizumab have comparable efficacy to the intravenous maintenance doses. In patients with severe disease, extended induction regimens up to 16 weeks or dose escalation may be beneficial for certain agents. In patients with moderate to severe UC naïve to advanced therapies, the AGA suggests using a higher efficacy medication (infliximab, vedolizumab, ozanimod, etrasimod, upadacitinib, risankizumab, guselkumab) or an intermediate efficacy medication (golimumab, ustekinumab, tofacitinib, filgotinib, mirikizumab), instead of a lower efficacy medication (adalimumab). JAK inhibitors may be associated with higher risk of major adverse cardiovascular events and cancer than TNF antagonists in older adults with cardiovascular risk factors. JAK inhibitors are recommended in those with failure or intolerance to TNF antagonists. Vedolizumab and anti-IL therapies may be associated with a lower infection risk than TNF antagonists and may be preferred in those at risk of immunosuppression-related infections or malignancies. JAK inhibitors and S1P receptor modulators should be avoided in women of childrearing age contemplating pregnancy.

Sarcoidosis
The European Respiratory Society Task Force has guidelines for treatment of pulmonary, cutaneous, cardiac, and neurologic sarcoidosis (*Baughman et al 2021*). Infliximab is a recommended therapy after continued disease or relapse while taking systemic corticosteroids and immunosuppressants (e.g., methotrexate, azathioprine, leflunomide, mycophenolate mofetil, hydroxychloroquine).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Remicade, and its biosimilars Avsola, Inflectra, Infliximab, and Renflexis are tumor necrosis factor (TNF) blockers indicated for:

- Crohn's Disease:
  - reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease 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 disease.
- 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 disease 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 disease 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 disease 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 adult patients with moderately to severely active disease.
- Ankylosing Spondylitis: reducing signs and symptoms in adult patients with active disease.

- Psoriatic Arthritis: reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients.
- Plaque Psoriasis: treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

Zymfentra is a tumor necrosis factor (TNF) blocker indicated in adults for maintenance treatment of:

- moderately to severely active ulcerative colitis following treatment with an infliximab product administered intravenously
- moderately to severely active Crohn's disease following treatment with an infliximab product administered intravenously.

References

1. Avsola (infliximab-axxq) for injection, for intravenous use [package insert] Amgen, Inc. Thousand Oaks, CA. September 2021.
2. Baughman RP, Drent M, Kavuru M, et al. Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement. *Am J Respir Crit Care Med*. 2006;174(7):795-802.
3. Baughman RP, Valeyre D, Korsten P, et al. ERS clinical practice guidelines on treatment of sarcoidosis. *Eur Respir J.* 2021;58(6):2004079.
4. Colombel JF, Hanauer SB, Sandborn W, et al. Subcutaneous infliximab (CT-P13 SC) as maintenance therapy for Crohn's disease: A phase 3, randomised, placebo-controlled study (LIBERTY-CD) [abstract]. *J Crohns Colitis*. 2023;17(1):i161-i162. Abstract DOP86.
5. Feuerstein JD, Ho EY, Shmidt E, et al. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. *Gastroenterology*. 2021;160(7):2496-2508.
6. Feuerstein JD, Isaacs KL, Schneider Y, Siddique SM, Falck-Ytter Y, Singh S; AGA Institute Clinical Guidelines Committee. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020 Apr;158(5):1450-1461. doi: 10.1053/j.gastro.2020.01.006. Epub 2020 Jan 13. PMID: 31945371; PMCID: PMC7175923.
7. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123
8. Gordon H, Minozzi S, Kopylov U, et al. ECCO guidelines on therapeutics in Crohn's disease: medical treatment. *JCC.* 2024;18:1531-1555. doi: 10.1093/ecco-jcc/jjae091.
9. Inflectra (infliximab-dyyb) for injection, for intravenous use [package insert] CELLTRION, Inc. Incheon, Republic of Korea. April 2023.
10. Infliximab- infliximab injection, powder, lyophilized, for solution [package insert] Janssen Biotech, Inc. Horsham, PA. March 2025.
11. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113(4):481-517.
12. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
13. Remicade (infliximab) for injection, for intravenous use [package insert] Janssen Biotech, Inc. Horsham, PA. February 2025.
14. Renflexis (infliximab-abda) for injection, for intravenous use [package insert] Samsung Bioepis Co., Ltd., Incheon, Republic of Korea. December 2023.

15. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
16. Sands BE, Hanauer SB, Colombel JF, et al. Subcutaneous infliximab (CT-P13 SC) as maintenance therapy for ulcerative colitis: A phase 3, randomized, placebo-controlled study: Results of the LIBERTY-UC study [abstract]. *J Crohns Colitis.* 2023;17(1):i163-i164. Abstract P492.
17. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Rheumatol*. 2019 Jan;71(1):5-32. doi: 10.1002/art.40726. Epub 2018 Nov 30. PMID: 30499246; PMCID: PMC8218333.
18. Singh S, Loftus EV, Limketkai BN, et al. AGA living clinical practice guideline on pharmacological management of moderate-to-severe ulcerative colitis. *Gastroenterology* 2024;167:1307-1343. doi: 10.1053/j.gastro.2024.10.001.
19. Ward MM, Deodhar A, Gensler LS, et al. 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2019;(10):1599-1613.
20. ZYMFENTRA (infliximab-dyyb) injection, for subcutaneous use [package insert] Celltrion USA, Inc. Jersey City, NJ. May 2025.

Policy History/Revision Information

Date	Summary of Changes
10/18/2023	Approved by OptumRx P&T Committee
10/16/2024	Annual Review. Added Zymfentra SC injection to policy. Update to clinical criteria to remove trial of anthralin and coal tar for plaque psoriasis. Updated HCPC codes, background, and references.
10/15/2025	Annual Review. Language changes made to background section without any change to clinical intent. Updates to background section, FDA section, and references.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

70021 07-24 ©2024 Aspirus Health Plan, Inc. All rights reserved.