Medical Benefit Drug Policy

# Infliximab (Avsola®, Inflectra®, Remicade®, Renflexis® & Zymfentra™)

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

Instructions for Use

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**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>.**

### 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
- 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

### 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

### 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**
- Minimum duration of a 4-week trial and failure, 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)
- 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

### 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.
- Trial and failure, contraindication, or intolerance to one of the following conventional therapies: **and**
  - 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

### 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

### 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
- 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

## 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 |
| 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 |

| ICD-10 Code | Description |
|---|---|
| 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 2021*). 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 2021*). 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 patient randomization, all patients received MTX (optimized to 20 mg/wk by Week 8) and either placebo, 3 mg/kg or 10 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≤0.001). 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 2021*) . 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 compa
patients receiving placebo. The PASI response was generally maintained throu

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 2021*). 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 a 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[illegible]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 2021*). 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 ...onse parameters) was achieved in 22% of Infliximab-treated patients vs. 1% in place... patients (...).

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 2021*). 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 see
mg/kg Infliximab group (P=0.002) and 56% (18/32) of patients in the 10 mg/kg
(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 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) in 50% and 18% of patients treated with Zymfentra and placebo, respectively (treatment difference 34, 95% CI: 23, 45; 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 2021*). 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 tr
Week 8. Of 32 patients taking concomitant immunomodulators at baseline, 23
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 [illegible] 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*).

**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*).

**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.

Infliximab is a tumor necrosis factor (TNF) blocker 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.

Remicade is a tumor necrosis factor (TNF) blocker 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.

Inflectra is a tumor necrosis factor (TNF) blocker 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 a
pediatric patients 6 years of age and older with moderately to severely ac[illegible]uate 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.

Avsola is a tumor necrosis factor (TNF) blocker 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.

Renflexis is a tumor necrosis factor (TNF) blocker 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 with moderately to severely active disease who have had an inadequate response to conventional therapy.

• **Ulcerative Colitis**: reducing signs and symptoms, inducing and maintaini ling, and eliminating corticosteroid use in adult patients with moderately to se n inadequate response to conventional therapy.
• **Pediatric Ulcerative Colitis**: reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 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 patients with moderately to severely active disease.
• **Ankylosing Spondylitis**: reducing signs and symptoms in patients with active disease.
• **Psoriatic Arthritis**: reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function.
• **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.

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## 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. |

## 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).