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

Policy Number: 2022D0004AK
Effective Date: March 1, 2022

Coverage Rationale

This policy refers to the following infliximab products:
- Avsola™ (infliximab-axxq)
- Inflectra® (infliximab-dyyb)
- Remicade® (infliximab)
- Renflexis® (infliximab-abda)
- Any FDA-approved infliximab biosimilar product not listed here*

*Any U.S. Food and Drug Administration approved and launched infliximab biosimilar product not listed by name in this policy will be considered non-preferred until reviewed by UnitedHealthcare.

Preferred Product

Medical Necessity Plans

Inflectra (infliximab-dyyb) and Avsola (infliximab-axxq) are the preferred infliximab products. Coverage will be provided for Inflectra or Avsola contingent on the coverage criteria in the Diagnosis-Specific Criteria section.

Coverage for Renflexis (infliximab-abda), Remicade (infliximab), or other non-preferred infliximab product will be provided contingent on the criteria in this section and the coverage criteria in the Diagnosis-Specific Criteria section. In order to continue coverage, members already on Remicade, Renflexis, or other non-preferred infliximab product will be required to change therapy to Inflectra or Avsola unless they meet the criteria in this section.

Preferred Product Criteria
(for Medicare reviews, refer to the CMS section**)

Treatment with Remicade, Renflexis, or other non-preferred infliximab biosimilar is medically necessary for the indications specified in this policy when one of the following criteria are met:
- Both of the following:

Related Commercial Policies
- Maximum Dosage and Frequency
- Provider Administered Drugs – Site of Care

Community Plan Policy
- Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®)

Related Medicare Advantage Policy
- Medicare Part B Step Therapy Programs
Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®)

UnitedHealthcare Commercial Medical Benefit Drug Policy

Effective 03/01/2022

Non-Medical Necessity Plans

Any infliximab product is to be approved contingent on the coverage criteria in the Diagnosis-Specific Criteria section.

Diagnosis-Specific Criteria

“Infliximab” will be used to refer to all infliximab products.

Infliximab is proven for the treatment of ankylosing spondylitis when all of the following criteria is met:1,57,62

- For initial therapy, all of the following:
  - Diagnosis of ankylosing spondylitis (AS); and
  - Infliximab is dosed according to U.S. Food and Drug Administration (FDA) labeled dosing for ankylosing spondylitis; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Initial authorization is for no more than 6 months

- For continuation of therapy, all of the following:
  - Documentation of positive clinical response to infliximab; and
  - Infliximab is dosed according to U.S. FDA labeled dosing for ankylosing spondylitis; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - For the preferred product: Reauthorization will be for no more than 12 months; or
  - For the non-preferred product: Reauthorization will be for no more than 6 months

Infliximab is medically necessary for the treatment of ankylosing spondylitis when all of the following criteria is met:1,57,62

- For initial therapy, all of the following:
  - Diagnosis of ankylosing spondylitis (AS); and
  - One of the following:
    - History of failure to two NSAIDs (e.g., ibuprofen, naproxen) at the maximally indicated doses, each used for at least 4 weeks within the last 3 months, unless contraindicated or clinically significant adverse effects are experienced; or
Patient is currently on Infliximab and
  o Infliximab is dosed according to U.S. Food and Drug Administration (FDA) labeled dosing for ankylosing spondylitis; and
  o Patient is not receiving infliximab in combination with any of the following:
    ▪ Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    ▪ Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
and
  o Prescribed by or in consultation with a rheumatologist; and
  o Initial authorization is for no more than 6 months

For continuation of therapy, all of the following:
  o Documentation of positive clinical response to infliximab; and
  o Infliximab is dosed according to U.S. FDA labeled dosing for ankylosing spondylitis; and
  o Patient is not receiving infliximab in combination with any of the following:
    ▪ Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    ▪ Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
and
  o Prescribed by or in consultation with a rheumatologist; and
  o For the preferred product: Reauthorization will be for no more than 12 months; or
  o For the non-preferred product: Reauthorization will be for no more than 6 months

Infliximab is proven and medically necessary for the treatment of Crohn’s disease when all of the following criteria is met:1,3-6,41,57, 62

For initial therapy, all of the following:
  o One of the following:
    ▪ Diagnosis of fistulizing Crohn’s disease (Crohn’s Disease Activity Index (CDAI) ≥ 220 and ≤ 400); or
    ▪ Both of the following:
      – Diagnosis of moderately to severely active Crohn’s disease; and
      – One of the following:
        ▪ History of failure to one of the following conventional therapies at up to maximally indicated doses within the last 3 months, unless contraindicated or clinically significant adverse effects are experienced:
          o Corticosteroids (e.g., prednisone, methylprednisolone, budesonide)
          o 6-mercaptopurine (Purinethol)
          o Azathioprine (Imuran)
          o Methotrexate (Rheumatrex, Trexall)
        or
        ▪ Patient is currently on Infliximab
and
  o Infliximab is dosed according to U.S. FDA labeled dosing for Crohn’s disease; and
  o Patient is not receiving infliximab in combination with any of the following:
    ▪ Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Entyvio (vedolizumab)]
    ▪ Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
and
  o Prescribed by or in consultation with a gastroenterologist; and
  o Initial authorization is for no more than 6 months

For continuation of therapy, all of the following:
  o Documentation of positive clinical response to infliximab; and
  o Infliximab is dosed according to U.S. FDA labeled dosing for Crohn’s disease; and
  o Patient is not receiving infliximab in combination with any of the following:
    ▪ Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Entyvio (vedolizumab)]
    ▪ Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®)

Page 4 of 39

UnitedHealthcare Commercial Medical Benefit Drug Policy

Effective 03/01/2022

Proprietary Information of UnitedHealthcare. Copyright 2022 United HealthCare Services, Inc.

Infliximab is proven and medically necessary for the treatment of noninfectious uveitis when all of the following criteria are met:12,14,15,17

- For initial therapy, all of the following:
  - Diagnosis of refractory noninfectious uveitis that is causing or threatening vision loss (e.g., noninfectious uveitis associated with Behçet’s or Reiter’s syndromes); and
  - History of failure, contraindication, or intolerance to all of the following:
    - Topical corticosteroids; and
    - Systemic corticosteroids; and
    - Immunosuppressive drugs (e.g., azathioprine, cyclosporine, or methotrexate) and
  - Infliximab is dosed no higher than 5 mg/kg, administered at week 0, 2, 6, and every 8 weeks thereafter; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)] and
  - Prescribed by or in consultation with one of the following:
    - Rheumatologist
    - Ophthalmologist
  - Initial authorization is for no more than 6 months

- For continuation of therapy, all of the following:
  - Documentation of positive clinical response to infliximab; and
  - Infliximab is dosed no higher than 5 mg/kg, administered every 8 weeks; and
  - Patient is not receiving infliximab in combination with either of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)] and
  - Prescribed by or in consultation with one of the following:
    - Rheumatologist
    - Ophthalmologist
  - For the preferred product: Reauthorization will be for no more than 12 months; or
  - For the non-preferred product: Reauthorization will be for no more than 6 months

Infliximab is proven for the treatment of plaque psoriasis when all of the following criteria are met:1,57,62

- For initial therapy, all of the following:
  - Diagnosis of chronic severe plaque psoriasis (i.e., extensive and/or disabling); and
  - Patient is a candidate for systemic therapy; and
  - Infliximab is dosed according to U.S. FDA labeled dosing for plaque psoriasis; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
    - Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] and
  - Initial authorization is for no more than 6 months

- For continuation of therapy, all of the following:
  - Documentation of positive clinical response to infliximab; and
Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®) 

UnitedHealthcare Commercial Medical Benefit Drug Policy 

Effective 03/01/2022 

Infliximab is dosed according to U.S. FDA labeled dosing for plaque psoriasis; and 

Patient is not receiving infliximab in combination with any of the following: 

- Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] 
- Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)] 
- Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] 

and 

For the preferred product: Reauthorization will be for no more than 12 months; or 
For the non-preferred product: Reauthorization will be for no more than 6 months 

Infliximab is medically necessary for the treatment of plaque psoriasis when all of the following criteria are met:1,57,62 

- For initial therapy, all of the following: 
  - Diagnosis of chronic severe plaque psoriasis (i.e., extensive and/or disabling); and 
  - One of the following: 
    - Greater than or equal to 3% body surface area involvement, palmoplantar, facial, genital involvement, or severe scalp psoriasis; and 
    - History of failure to one of the following topical therapies, unless contraindicated or clinically significant adverse effects are experienced: 
      - Corticosteroids (e.g., betamethasone, clobetasol, desonide) 
      - Vitamin D analogs (e.g., calcitriol, calcipotriene) 
      - Tazarotene 
      - Calcineurin inhibitors (e.g., tacrolimus, pimecrolimus) 
      - Anthralin 
      - Coal tar 
    - History of failure to a 3-month trial of methotrexate at the maximally indicated dose within the last 6 months, unless contraindicated or clinically significant adverse effects are experienced or 
      - Patient is currently on Infliximab 

and 

- Infliximab is dosed according to U.S. FDA labeled dosing for plaque psoriasis; and 
- Patient is not receiving infliximab in combination with any of the following: 
  - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] 
  - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)] 
  - Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] 

and 

- Prescribed by or in consultation with a dermatologist; and 
- Initial authorization is for no more than 6 months 

- For continuation of therapy, all of the following: 
  - Documentation of positive clinical response to infliximab; and 
  - Infliximab is dosed according to U.S. FDA labeled dosing for plaque psoriasis; and 
  - Patient is not receiving infliximab in combination with any of the following: 
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)] 
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)] 
    - Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)] 

and 

- Prescribed by or in consultation with a dermatologist; and 
- For the preferred product: Reauthorization will be for no more than 12 months; or 
- For the non-preferred product: Reauthorization will be for no more than 6 months 

Infliximab is proven for the treatment of psoriatic arthritis when all of the following criteria are met:1,57,62 

- For initial therapy, all of the following: 

Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®) 
UnitedHealthcare Commercial Medical Benefit Drug Policy 
Proprietary Information of UnitedHealthcare. Copyright 2022 United HealthCare Services, Inc.
Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®)

Infliximab is medically necessary for the treatment of psoriatic arthritis when all of the following criteria are met:1,57,62

For initial therapy, all of the following:
- Diagnosis of psoriatic arthritis (PsA); and
- One of the following:
  - History of failure to a 3-month trial of methotrexate at the maximally indicated dose within the last 6 months, unless contraindicated or clinically significant adverse effects are experienced; or
  - Patient is currently on Infliximab

For continuation of therapy, all of the following:
- Documentation of positive clinical response to infliximab; and
- Infliximab is dosed according to U.S. FDA labeled dosing for psoriatic arthritis; and
- Patient is not receiving infliximab in combination with any of the following:
  - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
  - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

- Prescribed by or in consultation with one of the following:
  - Rheumatologist
  - Dermatologist

- Initial authorization is for no more than 6 months

For the preferred product: Reauthorization will be for no more than 12 months; or

For the non-preferred product: Reauthorization will be for no more than 6 months
Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®)

For initial therapy, all of the following:
- Diagnosis of moderately to severely active rheumatoid arthritis (RA); and
- One of the following:
  - Patient is receiving concurrent therapy with methotrexate.
  - History of contraindication or intolerance to methotrexate.
  - Infliximab is dosed according to U.S. FDA labeled dosing for rheumatoid arthritis; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Initial authorization is for no more than 6 months

For continuation of therapy, all of the following:
- Documentation of positive clinical response to infliximab; and
- Infliximab is dosed according to U.S. FDA labeled dosing for rheumatoid arthritis; and
- Patient is not receiving infliximab in combination with any of the following:
  - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
  - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Prescribed by or in consultation with a rheumatologist; and
- Initial authorization is for no more than 6 months

For the preferred product: Reauthorization will be for no more than 12 months; or
For the non-preferred product: Reauthorization will be for no more than 6 months

Infliximab is medically necessary for the treatment of rheumatoid arthritis when all of the following criteria are met:

For initial therapy, all of the following:
- Diagnosis of moderately to severely active rheumatoid arthritis (RA); and
- One of the following:
  - History of failure intolerance to a 3 month trial of one non-biologic disease modifying anti-rheumatic drug (DMARD) [e.g., methotrexate, leflunomide, sulfasalazine, hydroxychloroquine] at maximally indicated doses within the last 6 months, unless contraindicated or clinically significant adverse effects are experienced; or
  - Patient is currently on infliximab
  - Infliximab is dosed according to U.S. FDA labeled dosing for rheumatoid arthritis; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
    - Prescribed by or in consultation with a rheumatologist; and
- Initial authorization is for no more than 6 months

For continuation of therapy, all of the following:
- Documentation of positive clinical response to infliximab; and
- Infliximab is dosed according to U.S. FDA labeled dosing for rheumatoid arthritis; and
- Patient is not receiving infliximab in combination with any of the following:
  - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
  - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Prescribed by or in consultation with a rheumatologist; and
  - For the preferred product: Reauthorization will be for no more than 12 months; or
  - For the non-preferred product: Reauthorization will be for no more than 6 months

For the non-preferred product: Reauthorization will be for no more than 6 months.
Infliximab is proven and medically necessary for the treatment of sarcoidosis when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of sarcoidosis; and
  - History of failure, contraindication, or intolerance to corticosteroids (e.g., prednisone, methylprednisolone); and
  - History of failure, contraindication, or intolerance to one immunosuppressant (e.g., methotrexate, cyclophosphamide, azathioprine); and
  - Infliximab is dosed no higher than 10 mg/kg, administered at week 0, 2, 6, and every 8 weeks thereafter; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Initial authorization is for no more than 6 months

- For continuation of therapy, all of the following:
  - Documentation of positive clinical response to infliximab; and
  - Infliximab is dosed no higher than 10 mg/kg, administered every 8 weeks; and
  - Patient is not receiving infliximab in combination with either of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - For the preferred product: Reauthorization will be for no more than 12 months; or
  - For the non-preferred product: Reauthorization will be for no more than 6 months

Infliximab is proven and medically necessary for the treatment of ulcerative colitis when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of moderately to severely active ulcerative colitis (UC); and
  - History of failure, contraindication, or intolerance to at least one conventional therapy (e.g., 6-mercaptopurine, aminosalicylate, azathioprine, corticosteroids); and
  - Infliximab is dosed according to U.S. FDA labeled dosing for UC; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Entyvio (vedolizumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Prescribed by or in consultation with a gastroenterologist; and
  - Initial authorization is for no more than 6 months

- For continuation of therapy, all of the following:
  - Documentation of positive clinical response to infliximab; and
  - Infliximab is dosed according to U.S. FDA labeled dosing for UC; and
  - Patient is not receiving infliximab in combination with any of the following:
    - Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Entyvio (vedolizumab)]
    - Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]
  - Prescribed by or in consultation with a gastroenterologist; and
  - For the preferred product: Reauthorization will be for no more than 12 months; or
  - For the non-preferred product: Reauthorization will be for no more than 6 months

Infliximab is proven and medically necessary for the treatment of acute graft-versus-host disease (GVHD) when all of the following criteria are met:

- For initial therapy, all of the following:
  - Diagnosis of steroid-refractory acute GVHD; and
o One of the following:
   ▪ Patient is receiving infliximab in combination with systemic corticosteroids
   ▪ Patient is intolerant to systemic corticosteroid therapy
   and

o Initial authorization is for no more than 4 doses

For continuation of therapy, all of the following:

o Documentation of positive clinical response; and
o Patient continues to experience acute GVHD; and
o One of the following:
   ▪ Patient is receiving infliximab in combination with systemic corticosteroids
   ▪ Patient is intolerant to systemic corticosteroid therapy
   and

o Reauthorization is for no more than 4 doses

Infliximab is proven and medically necessary for the treatment of Immune checkpoint inhibitor-related toxicities when all of the following criteria are met:67

For initial therapy, all of the following:

● Patient has recently received checkpoint inhibitor therapy [e.g., Keytruda (Pembrolizumab), Opdivo (Nivolumab)]; and
● Diagnosis of one of the following:
   ○ Moderate (G2) or severe (G3-4) immunotherapy-related diarrhea or colitis;
   ○ Severe (G3-4) immunotherapy-related pneumonitis;
   ○ Severe (G3) or life-threatening (G4) immunotherapy-related acute renal failure/elevated serum creatinine; severe (G3-4) immunotherapy-related uveitis;
   ○ Life threatening (G4) immunotherapy-related myocarditis, pericarditis, arrhythmias, impaired ventricular function, or conduction abnormalities;
   ○ Severe immunotherapy-related inflammatory arthritis;
   ○ Moderate, severe, or life-threatening immunotherapy-related, steroid-refractory myalgias or myositis (muscle weakness)
   and
● Patient has had inadequate improvement in toxicities or symptoms despite systemic corticosteroid therapy of adequate dose and duration for the diagnosis; and
● One of the following:
   ○ Patient is receiving infliximab in combination with systemic corticosteroids
   ○ Patient is intolerant to systemic corticosteroid therapy
   and
● Initial authorization is for no more than 4 doses

For continuation of therapy, all of the following:

o Documentation of positive clinical response; and
o Patient continues to experience toxicities from treatment with immune checkpoint inhibitor therapy; and
o One of the following:
   ▪ Patient is receiving infliximab in combination with systemic corticosteroids
   ▪ Patient is intolerant to systemic corticosteroid therapy
   and
o Reauthorization is for no more than 4 doses

There may be other conditions that qualify as serious, rare diseases for which the use of infliximab may be appropriate. Refer to the Benefit Considerations section of this policy for additional information.

Infliximab is unproven and not medically necessary for the treatment of:

● Hidradenitis suppurativa
● Juvenile idiopathic arthritis (juvenile rheumatoid arthritis)
● Myelodysplastic syndromes
● Reiter’s syndrome
● Sjögren’s syndrome
● Still’s disease
● Undifferentiated spondyloarthropathy
● Wegener’s granulomatosis

Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®)
UnitedHealthcare Commercial Medical Benefit Drug Policy

Page 9 of 39
Effective 03/01/2022

Proprietary Information of UnitedHealthcare. Copyright 2022 United HealthCare Services, Inc.
Infliximab is unproven for the treatment of the above conditions because statistically robust randomized controlled trials are needed to address the issue of whether infliximab has sufficient superiority in clinical efficacy compared to other available treatments to justify the inherent clinical risk in the use of a monoclonal antibody anti-tumor necrosis factor agent.

### Documentation Requirements

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 documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage, but do not guarantee coverage of the service requested.

<table>
<thead>
<tr>
<th>HCPCS Code*</th>
<th>Required Clinical Information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Remicade®, Renflexis®, Ixifi ™</strong></td>
<td></td>
</tr>
</tbody>
</table>
| J1745, Q5104, Q5109 | For initial and continuation of therapy requests, medical notes documenting one of the following:  
  - Both of the following:  
    - History of a trial of at least 14 weeks of Inflectra or Avsola resulting in minimal clinical response to therapy and residual disease activity; and  
    - Physician attests that in their clinical opinion, the clinical response would be expected to be superior with Remicade, Renflexis, or other infliximab biosimilar product, than experienced with Inflectra and Avsola.  
  or  
  - Both of the following:  
    - Documentation of intolerance, contraindication, or adverse event to Inflectra or Avsola; and  
    - Physician attests that in their clinical opinion, the same intolerance, contraindication, or adverse event would not be expected to occur with Remicade, Renflexis, or other infliximab biosimilar product. |

*For code description, refer to the **Applicable Codes** section.

### 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.

Coding Clarification: HCPCS code Q5109 is provided for informational purposes only. Ixifi™ (infliximab-qbtx) is currently unavailable in the USA.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J1745</td>
<td>Injection, infliximab, excludes biosimilar, 10 mg</td>
</tr>
<tr>
<td>Q5103</td>
<td>Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg</td>
</tr>
<tr>
<td>Q5104</td>
<td>Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg</td>
</tr>
<tr>
<td>Q5109</td>
<td>Injection, infliximab-qbtx, biosimilar, (Ixifi), 10 mg</td>
</tr>
<tr>
<td>Q5121</td>
<td>Injection, infliximab-axxq, biosimilar, (Avsola), 10 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D86.0</td>
<td>Sarcoidosis of lung</td>
</tr>
<tr>
<td>D86.1</td>
<td>Sarcoidosis of lymph nodes</td>
</tr>
<tr>
<td>D86.2</td>
<td>Sarcoidosis of lung with sarcoidosis of lymph nodes</td>
</tr>
<tr>
<td>D86.3</td>
<td>Sarcoidosis of skin</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>D86.81</td>
<td>Sarcoid meningitis</td>
</tr>
<tr>
<td>D86.82</td>
<td>Multiple cranial nerve palsies in sarcoidosis</td>
</tr>
<tr>
<td>D86.83</td>
<td>Sarcoid iridocyclitis</td>
</tr>
<tr>
<td>D86.84</td>
<td>Sarcoid pyelonephritis</td>
</tr>
<tr>
<td>D86.85</td>
<td>Sarcoid myocarditis</td>
</tr>
<tr>
<td>D86.86</td>
<td>Sarcoid arthropathy</td>
</tr>
<tr>
<td>D86.87</td>
<td>Sarcoid myositis</td>
</tr>
<tr>
<td>D86.89</td>
<td>Sarcoidosis of other sites</td>
</tr>
<tr>
<td>D86.9</td>
<td>Sarcoidosis, unspecified</td>
</tr>
<tr>
<td>D89.810</td>
<td>Acute graft-versus-host disease</td>
</tr>
<tr>
<td>H20.041</td>
<td>Secondary noninfectious iridocyclitis, right eye</td>
</tr>
<tr>
<td>H20.042</td>
<td>Secondary noninfectious iridocyclitis, left eye</td>
</tr>
<tr>
<td>H20.043</td>
<td>Secondary noninfectious iridocyclitis, bilateral</td>
</tr>
<tr>
<td>H20.049</td>
<td>Secondary noninfectious iridocyclitis, unspecified eye</td>
</tr>
<tr>
<td>H20.10</td>
<td>Chronic iridocyclitis, unspecified eye</td>
</tr>
<tr>
<td>H20.11</td>
<td>Chronic iridocyclitis, right eye</td>
</tr>
<tr>
<td>H20.12</td>
<td>Chronic iridocyclitis, left eye</td>
</tr>
<tr>
<td>H20.13</td>
<td>Chronic iridocyclitis, bilateral</td>
</tr>
<tr>
<td>H20.821</td>
<td>Vogt-Koyanagi syndrome, right eye</td>
</tr>
<tr>
<td>H20.822</td>
<td>Vogt-Koyanagi syndrome, left eye</td>
</tr>
<tr>
<td>H20.823</td>
<td>Vogt-Koyanagi syndrome, bilateral</td>
</tr>
<tr>
<td>H20.829</td>
<td>Vogt-Koyanagi syndrome, unspecified eye</td>
</tr>
<tr>
<td>H30.001</td>
<td>Unspecified focal chorioretinal inflammation, right eye</td>
</tr>
<tr>
<td>H30.002</td>
<td>Unspecified focal chorioretinal inflammation, left eye</td>
</tr>
<tr>
<td>H30.003</td>
<td>Unspecified focal chorioretinal inflammation, bilateral</td>
</tr>
<tr>
<td>H30.009</td>
<td>Unspecified focal chorioretinal inflammation, unspecified eye</td>
</tr>
<tr>
<td>H30.011</td>
<td>Focal chorioretinal inflammation, juxtapapillary, right eye</td>
</tr>
<tr>
<td>H30.012</td>
<td>Focal chorioretinal inflammation, juxtapapillary, left eye</td>
</tr>
<tr>
<td>H30.013</td>
<td>Focal chorioretinal inflammation, juxtapapillary, bilateral</td>
</tr>
<tr>
<td>H30.019</td>
<td>Focal chorioretinal inflammation, juxtapapillary, unspecified eye</td>
</tr>
<tr>
<td>H30.021</td>
<td>Focal chorioretinal inflammation of posterior pole, right eye</td>
</tr>
<tr>
<td>H30.022</td>
<td>Focal chorioretinal inflammation of posterior pole, left eye</td>
</tr>
<tr>
<td>H30.023</td>
<td>Focal chorioretinal inflammation of posterior pole, bilateral</td>
</tr>
<tr>
<td>H30.029</td>
<td>Focal chorioretinal inflammation of posterior pole, unspecified eye</td>
</tr>
<tr>
<td>H30.031</td>
<td>Focal chorioretinal inflammation, peripheral, right eye</td>
</tr>
<tr>
<td>H30.032</td>
<td>Focal chorioretinal inflammation, peripheral, left eye</td>
</tr>
<tr>
<td>H30.033</td>
<td>Focal chorioretinal inflammation, peripheral, bilateral</td>
</tr>
<tr>
<td>H30.039</td>
<td>Focal chorioretinal inflammation, peripheral, unspecified eye</td>
</tr>
<tr>
<td>H30.041</td>
<td>Focal chorioretinal inflammation, macular or paramacular, right eye</td>
</tr>
<tr>
<td>H30.042</td>
<td>Focal chorioretinal inflammation, macular or paramacular, left eye</td>
</tr>
<tr>
<td>H30.043</td>
<td>Focal chorioretinal inflammation, macular or paramacular, bilateral</td>
</tr>
<tr>
<td>H30.049</td>
<td>Focal chorioretinal inflammation, macular or paramacular, unspecified eye</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>H30.101</td>
<td>Unspecified disseminated chorioretinal inflammation (chorioretinitis/choroiditis), right eye</td>
</tr>
<tr>
<td>H30.102</td>
<td>Unspecified disseminated chorioretinal inflammation (chorioretinitis/choroiditis), left eye</td>
</tr>
<tr>
<td>H30.103</td>
<td>Unspecified disseminated chorioretinal inflammation (chorioretinitis/choroiditis), bilateral</td>
</tr>
<tr>
<td>H30.109</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis), unspecified eye</td>
</tr>
<tr>
<td>H30.111</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis) posterior pole, right eye</td>
</tr>
<tr>
<td>H30.112</td>
<td>Disseminated chorioretinal inflammation (choroiditis/chorioretinitis) posterior pole, left eye</td>
</tr>
<tr>
<td>H30.113</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis) posterior pole, bilateral</td>
</tr>
<tr>
<td>H30.119</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis) posterior pole, unspecified eye</td>
</tr>
<tr>
<td>H30.121</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis) peripheral, right eye</td>
</tr>
<tr>
<td>H30.122</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis) peripheral, left eye</td>
</tr>
<tr>
<td>H30.123</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis) peripheral, bilateral</td>
</tr>
<tr>
<td>H30.129</td>
<td>Disseminated chorioretinal inflammation (chorioretinitis/choroiditis) peripheral, unspecified eye</td>
</tr>
<tr>
<td>H30.131</td>
<td>Disseminated chorioretinal inflammation, generalized, right eye</td>
</tr>
<tr>
<td>H30.132</td>
<td>Disseminated chorioretinal inflammation, generalized, left eye</td>
</tr>
<tr>
<td>H30.133</td>
<td>Disseminated chorioretinal inflammation, generalized, bilateral</td>
</tr>
<tr>
<td>H30.139</td>
<td>Disseminated chorioretinal inflammation, generalized, unspecified eye</td>
</tr>
<tr>
<td>H30.20</td>
<td>Posterior cyclitis, unspecified eye</td>
</tr>
<tr>
<td>H30.21</td>
<td>Posterior cyclitis, right eye</td>
</tr>
<tr>
<td>H30.22</td>
<td>Posterior cyclitis, left eye</td>
</tr>
<tr>
<td>H30.23</td>
<td>Posterior cyclitis, bilateral</td>
</tr>
<tr>
<td>H30.811</td>
<td>Harada’s disease, right eye</td>
</tr>
<tr>
<td>H30.812</td>
<td>Harada’s disease, left eye</td>
</tr>
<tr>
<td>H30.813</td>
<td>Harada’s disease, bilateral</td>
</tr>
<tr>
<td>H30.819</td>
<td>Harada’s disease, unspecified eye</td>
</tr>
<tr>
<td>H30.891</td>
<td>Other chorioretinal inflammations, right eye</td>
</tr>
<tr>
<td>H30.892</td>
<td>Other chorioretinal inflammations, left eye</td>
</tr>
<tr>
<td>H30.893</td>
<td>Other chorioretinal inflammations, bilateral</td>
</tr>
<tr>
<td>H30.899</td>
<td>Other chorioretinal inflammations, unspecified eye</td>
</tr>
<tr>
<td>H30.90</td>
<td>Unspecified chorioretinal inflammation, unspecified eye</td>
</tr>
<tr>
<td>H30.91</td>
<td>Unspecified chorioretinal inflammation, right eye</td>
</tr>
<tr>
<td>H30.92</td>
<td>Unspecified chorioretinal inflammation, left eye</td>
</tr>
<tr>
<td>H30.93</td>
<td>Unspecified chorioretinal inflammation, bilateral</td>
</tr>
<tr>
<td>H35.021</td>
<td>Exudative retinopathy, right eye</td>
</tr>
<tr>
<td>H35.022</td>
<td>Exudative retinopathy, left eye</td>
</tr>
<tr>
<td>H35.023</td>
<td>Exudative retinopathy, bilateral</td>
</tr>
<tr>
<td>H35.029</td>
<td>Exudative retinopathy, unspecified eye</td>
</tr>
<tr>
<td>H35.061</td>
<td>Retinal vasculitis, right eye</td>
</tr>
<tr>
<td>H35.062</td>
<td>Retinal vasculitis, left eye</td>
</tr>
<tr>
<td>H35.063</td>
<td>Retinal vasculitis, bilateral</td>
</tr>
<tr>
<td>H35.069</td>
<td>Retinal vasculitis, unspecified eye</td>
</tr>
<tr>
<td>H44.111</td>
<td>Panuveitis, right eye</td>
</tr>
<tr>
<td>H44.112</td>
<td>Panuveitis, left eye</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>H44.113</td>
<td>Panuveitis, bilateral</td>
</tr>
<tr>
<td>H44.119</td>
<td>Panuveitis, unspecified eye</td>
</tr>
<tr>
<td>H44.131</td>
<td>Sympathetic uveitis, right eye</td>
</tr>
<tr>
<td>H44.132</td>
<td>Sympathetic uveitis, left eye</td>
</tr>
<tr>
<td>H44.133</td>
<td>Sympathetic uveitis, bilateral</td>
</tr>
<tr>
<td>H44.139</td>
<td>Sympathetic uveitis, unspecified eye</td>
</tr>
<tr>
<td>I30.8</td>
<td>Other forms of acute pericarditis</td>
</tr>
<tr>
<td>I30.9</td>
<td>Acute pericarditis, unspecified</td>
</tr>
<tr>
<td>I40.8</td>
<td>Other acute myocarditis</td>
</tr>
<tr>
<td>I40.9</td>
<td>Acute myocarditis, unspecified</td>
</tr>
<tr>
<td>I50.9</td>
<td>Heart failure, unspecified</td>
</tr>
<tr>
<td>J70.2</td>
<td>Acute drug-induced interstitial lung disorders</td>
</tr>
<tr>
<td>J70.4</td>
<td>Drug-induced interstitial lung disorders, unspecified</td>
</tr>
<tr>
<td>K31.6</td>
<td>Fistula of stomach and duodenum</td>
</tr>
<tr>
<td>K50.00</td>
<td>Crohn’s disease of small intestine without complications</td>
</tr>
<tr>
<td>K50.011</td>
<td>Crohn’s disease of small intestine with rectal bleeding</td>
</tr>
<tr>
<td>K50.012</td>
<td>Crohn’s disease of small intestine with intestinal obstruction</td>
</tr>
<tr>
<td>K50.013</td>
<td>Crohn’s disease of small intestine with fistula</td>
</tr>
<tr>
<td>K50.014</td>
<td>Crohn’s disease of small intestine with abscess</td>
</tr>
<tr>
<td>K50.018</td>
<td>Crohn’s disease of small intestine with other complication</td>
</tr>
<tr>
<td>K50.019</td>
<td>Crohn’s disease of small intestine with unspecified complications</td>
</tr>
<tr>
<td>K50.10</td>
<td>Crohn’s disease of large intestine without complications</td>
</tr>
<tr>
<td>K50.111</td>
<td>Crohn’s disease of large intestine with rectal bleeding</td>
</tr>
<tr>
<td>K50.112</td>
<td>Crohn’s disease of large intestine with intestinal obstruction</td>
</tr>
<tr>
<td>K50.113</td>
<td>Crohn’s disease of large intestine with fistula</td>
</tr>
<tr>
<td>K50.114</td>
<td>Crohn’s disease of large intestine with abscess</td>
</tr>
<tr>
<td>K50.118</td>
<td>Crohn’s disease of large intestine with other complication</td>
</tr>
<tr>
<td>K50.119</td>
<td>Crohn’s disease of large intestine with unspecified complications</td>
</tr>
<tr>
<td>K50.80</td>
<td>Crohn’s disease of both small and large intestine without complications</td>
</tr>
<tr>
<td>K50.811</td>
<td>Crohn’s disease of both small and large intestine with rectal bleeding</td>
</tr>
<tr>
<td>K50.812</td>
<td>Crohn’s disease of both small and large intestine with intestinal obstruction</td>
</tr>
<tr>
<td>K50.813</td>
<td>Crohn’s disease of both small and large intestine with fistula</td>
</tr>
<tr>
<td>K50.814</td>
<td>Crohn’s disease of both small and large intestine with abscess</td>
</tr>
<tr>
<td>K50.818</td>
<td>Crohn’s disease of both small and large intestine with other complication</td>
</tr>
<tr>
<td>K50.819</td>
<td>Crohn’s disease of both small and large intestine with unspecified complications</td>
</tr>
<tr>
<td>K50.90</td>
<td>Crohn’s disease, unspecified, without complications</td>
</tr>
<tr>
<td>K50.911</td>
<td>Crohn’s disease, unspecified, with rectal bleeding</td>
</tr>
<tr>
<td>K50.912</td>
<td>Crohn’s disease, unspecified, with intestinal obstruction</td>
</tr>
<tr>
<td>K50.913</td>
<td>Crohn’s disease, unspecified, with fistula</td>
</tr>
<tr>
<td>K50.914</td>
<td>Crohn’s disease, unspecified, with abscess</td>
</tr>
<tr>
<td>K50.918</td>
<td>Crohn’s disease, unspecified, with other complication</td>
</tr>
<tr>
<td>K50.919</td>
<td>Crohn’s disease, unspecified, with unspecified complications</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>K51.00</td>
<td>Ulcerative (chronic) pancolitis without complications</td>
</tr>
<tr>
<td>K51.011</td>
<td>Ulcerative (chronic) pancolitis with rectal bleeding</td>
</tr>
<tr>
<td>K51.012</td>
<td>Ulcerative (chronic) pancolitis with intestinal obstruction</td>
</tr>
<tr>
<td>K51.013</td>
<td>Ulcerative (chronic) pancolitis with fistula</td>
</tr>
<tr>
<td>K51.014</td>
<td>Ulcerative (chronic) pancolitis with abscess</td>
</tr>
<tr>
<td>K51.018</td>
<td>Ulcerative (chronic) pancolitis with other complication</td>
</tr>
<tr>
<td>K51.019</td>
<td>Ulcerative (chronic) pancolitis with unspecified complications</td>
</tr>
<tr>
<td>K51.20</td>
<td>Ulcerative (chronic) proctitis without complications</td>
</tr>
<tr>
<td>K51.211</td>
<td>Ulcerative (chronic) proctitis with rectal bleeding</td>
</tr>
<tr>
<td>K51.212</td>
<td>Ulcerative (chronic) proctitis with intestinal obstruction</td>
</tr>
<tr>
<td>K51.213</td>
<td>Ulcerative (chronic) proctitis with fistula</td>
</tr>
<tr>
<td>K51.214</td>
<td>Ulcerative (chronic) proctitis with abscess</td>
</tr>
<tr>
<td>K51.218</td>
<td>Ulcerative (chronic) proctitis with other complication</td>
</tr>
<tr>
<td>K51.219</td>
<td>Ulcerative (chronic) proctitis with unspecified complications</td>
</tr>
<tr>
<td>K51.30</td>
<td>Ulcerative (chronic) rectosigmoiditis without complications</td>
</tr>
<tr>
<td>K51.311</td>
<td>Ulcerative (chronic) rectosigmoiditis with rectal bleeding</td>
</tr>
<tr>
<td>K51.312</td>
<td>Ulcerative (chronic) rectosigmoiditis with intestinal obstruction</td>
</tr>
<tr>
<td>K51.313</td>
<td>Ulcerative (chronic) rectosigmoiditis with fistula</td>
</tr>
<tr>
<td>K51.314</td>
<td>Ulcerative (chronic) rectosigmoiditis with abscess</td>
</tr>
<tr>
<td>K51.318</td>
<td>Ulcerative (chronic) rectosigmoiditis with other complication</td>
</tr>
<tr>
<td>K51.319</td>
<td>Ulcerative (chronic) rectosigmoiditis with unspecified complications</td>
</tr>
<tr>
<td>K51.40</td>
<td>Inflammatory polyps of colon without complications</td>
</tr>
<tr>
<td>K51.411</td>
<td>Inflammatory polyps of colon with rectal bleeding</td>
</tr>
<tr>
<td>K51.412</td>
<td>Inflammatory polyps of colon with intestinal obstruction</td>
</tr>
<tr>
<td>K51.413</td>
<td>Inflammatory polyps of colon with fistula</td>
</tr>
<tr>
<td>K51.414</td>
<td>Inflammatory polyps of colon with abscess</td>
</tr>
<tr>
<td>K51.418</td>
<td>Inflammatory polyps of colon with other complication</td>
</tr>
<tr>
<td>K51.419</td>
<td>Inflammatory polyps of colon with unspecified complications</td>
</tr>
<tr>
<td>K51.50</td>
<td>Left sided colitis without complications</td>
</tr>
<tr>
<td>K51.511</td>
<td>Left sided colitis with rectal bleeding</td>
</tr>
<tr>
<td>K51.512</td>
<td>Left sided colitis with intestinal obstruction</td>
</tr>
<tr>
<td>K51.513</td>
<td>Left sided colitis with fistula</td>
</tr>
<tr>
<td>K51.514</td>
<td>Left sided colitis with abscess</td>
</tr>
<tr>
<td>K51.518</td>
<td>Left sided colitis with other complication</td>
</tr>
<tr>
<td>K51.519</td>
<td>Left sided colitis with unspecified complications</td>
</tr>
<tr>
<td>K51.80</td>
<td>Other ulcerative colitis without complications</td>
</tr>
<tr>
<td>K51.811</td>
<td>Other ulcerative colitis with rectal bleeding</td>
</tr>
<tr>
<td>K51.812</td>
<td>Other ulcerative colitis with intestinal obstruction</td>
</tr>
<tr>
<td>K51.813</td>
<td>Other ulcerative colitis with fistula</td>
</tr>
<tr>
<td>K51.814</td>
<td>Other ulcerative colitis with abscess</td>
</tr>
<tr>
<td>K51.818</td>
<td>Other ulcerative colitis with other complication</td>
</tr>
<tr>
<td>K51.819</td>
<td>Other ulcerative colitis with unspecified complications</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------</td>
</tr>
<tr>
<td>K51.90</td>
<td>Ulcerative colitis, unspecified, without complications</td>
</tr>
<tr>
<td>K51.911</td>
<td>Ulcerative colitis, unspecified with rectal bleeding</td>
</tr>
<tr>
<td>K51.912</td>
<td>Ulcerative colitis, unspecified with intestinal obstruction</td>
</tr>
<tr>
<td>K51.913</td>
<td>Ulcerative colitis, unspecified with fistula</td>
</tr>
<tr>
<td>K51.914</td>
<td>Ulcerative colitis, unspecified with abscess</td>
</tr>
<tr>
<td>K51.918</td>
<td>Ulcerative colitis, unspecified with other complication</td>
</tr>
<tr>
<td>K51.919</td>
<td>Ulcerative colitis, unspecified with unspecified complications</td>
</tr>
<tr>
<td>K52.1</td>
<td>Toxic gastroenteritis and colitis</td>
</tr>
<tr>
<td>K60.3</td>
<td>Anal fistula</td>
</tr>
<tr>
<td>K60.4</td>
<td>Rectal fistula</td>
</tr>
<tr>
<td>K60.5</td>
<td>Anorectal fistula</td>
</tr>
<tr>
<td>K63.2</td>
<td>Fistula of intestine</td>
</tr>
<tr>
<td>L40.0</td>
<td>Psoriasis vulgaris</td>
</tr>
<tr>
<td>L40.1</td>
<td>Generalized pustular psoriasis</td>
</tr>
<tr>
<td>L40.2</td>
<td>Acrodermatitis continua</td>
</tr>
<tr>
<td>L40.3</td>
<td>Pustulosis palmaris et plantaris</td>
</tr>
<tr>
<td>L40.4</td>
<td>Guttate psoriasis</td>
</tr>
<tr>
<td>L40.50</td>
<td>Arthropathic psoriasis, unspecified</td>
</tr>
<tr>
<td>L40.51</td>
<td>Distal interphalangeal psoriatic arthropathy</td>
</tr>
<tr>
<td>L40.52</td>
<td>Psoriatic arthritis mutilans</td>
</tr>
<tr>
<td>L40.53</td>
<td>Psoriatic spondylitis</td>
</tr>
<tr>
<td>L40.54</td>
<td>Psoriatic juvenile arthropathy</td>
</tr>
<tr>
<td>L40.59</td>
<td>Other psoriatic arthropathy</td>
</tr>
<tr>
<td>L40.8</td>
<td>Other psoriasis</td>
</tr>
<tr>
<td>L40.9</td>
<td>Psoriasis, unspecified</td>
</tr>
<tr>
<td>M05.00</td>
<td>Felty’s syndrome, unspecified site</td>
</tr>
<tr>
<td>M05.011</td>
<td>Felty’s syndrome, right shoulder</td>
</tr>
<tr>
<td>M05.012</td>
<td>Felty’s syndrome, left shoulder</td>
</tr>
<tr>
<td>M05.019</td>
<td>Felty’s syndrome, unspecified shoulder</td>
</tr>
<tr>
<td>M05.021</td>
<td>Felty’s syndrome, right elbow</td>
</tr>
<tr>
<td>M05.022</td>
<td>Felty’s syndrome, left elbow</td>
</tr>
<tr>
<td>M05.029</td>
<td>Felty’s syndrome, unspecified elbow</td>
</tr>
<tr>
<td>M05.031</td>
<td>Felty’s syndrome, right wrist</td>
</tr>
<tr>
<td>M05.032</td>
<td>Felty’s syndrome, left wrist</td>
</tr>
<tr>
<td>M05.039</td>
<td>Felty’s syndrome, unspecified wrist</td>
</tr>
<tr>
<td>M05.041</td>
<td>Felty’s syndrome, right hand</td>
</tr>
<tr>
<td>M05.042</td>
<td>Felty’s syndrome, left hand</td>
</tr>
<tr>
<td>M05.049</td>
<td>Felty’s syndrome, unspecified hand</td>
</tr>
<tr>
<td>M05.051</td>
<td>Felty’s syndrome, right hip</td>
</tr>
<tr>
<td>M05.052</td>
<td>Felty’s syndrome, left hip</td>
</tr>
<tr>
<td>M05.059</td>
<td>Felty’s syndrome, unspecified hip</td>
</tr>
<tr>
<td>M05.061</td>
<td>Felty’s syndrome, right knee</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------</td>
</tr>
<tr>
<td>M05.062</td>
<td>Felty’s syndrome, left knee</td>
</tr>
<tr>
<td>M05.069</td>
<td>Felty’s syndrome, unspecified knee</td>
</tr>
<tr>
<td>M05.071</td>
<td>Felty’s syndrome, right ankle and foot</td>
</tr>
<tr>
<td>M05.072</td>
<td>Felty’s syndrome, left ankle and foot</td>
</tr>
<tr>
<td>M05.079</td>
<td>Felty’s syndrome, unspecified ankle and foot</td>
</tr>
<tr>
<td>M05.09</td>
<td>Felty’s syndrome, multiple sites</td>
</tr>
<tr>
<td>M05.20</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified site</td>
</tr>
<tr>
<td>M05.211</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of right shoulder</td>
</tr>
<tr>
<td>M05.212</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of left shoulder</td>
</tr>
<tr>
<td>M05.219</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified shoulder</td>
</tr>
<tr>
<td>M05.221</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of right elbow</td>
</tr>
<tr>
<td>M05.222</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of left elbow</td>
</tr>
<tr>
<td>M05.229</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified elbow</td>
</tr>
<tr>
<td>M05.231</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of right wrist</td>
</tr>
<tr>
<td>M05.232</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of left wrist</td>
</tr>
<tr>
<td>M05.239</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified wrist</td>
</tr>
<tr>
<td>M05.241</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of right hand</td>
</tr>
<tr>
<td>M05.242</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of left hand</td>
</tr>
<tr>
<td>M05.249</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified hand</td>
</tr>
<tr>
<td>M05.251</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of right hip</td>
</tr>
<tr>
<td>M05.252</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of left hip</td>
</tr>
<tr>
<td>M05.259</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified hip</td>
</tr>
<tr>
<td>M05.261</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of right knee</td>
</tr>
<tr>
<td>M05.262</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of left knee</td>
</tr>
<tr>
<td>M05.269</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified knee</td>
</tr>
<tr>
<td>M05.271</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot</td>
</tr>
<tr>
<td>M05.272</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot</td>
</tr>
<tr>
<td>M05.279</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of unspecified ankle and foot</td>
</tr>
<tr>
<td>M05.29</td>
<td>Rheumatoid vasculitis with rheumatoid arthritis of multiple sites</td>
</tr>
<tr>
<td>M05.30</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified site</td>
</tr>
<tr>
<td>M05.311</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of right shoulder</td>
</tr>
<tr>
<td>M05.312</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of left shoulder</td>
</tr>
<tr>
<td>M05.319</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified shoulder</td>
</tr>
<tr>
<td>M05.321</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of right elbow</td>
</tr>
<tr>
<td>M05.322</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of left elbow</td>
</tr>
<tr>
<td>M05.329</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified elbow</td>
</tr>
<tr>
<td>M05.331</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of right wrist</td>
</tr>
<tr>
<td>M05.332</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of left wrist</td>
</tr>
<tr>
<td>M05.339</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified wrist</td>
</tr>
<tr>
<td>M05.341</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of right hand</td>
</tr>
<tr>
<td>M05.342</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of left hand</td>
</tr>
<tr>
<td>M05.349</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified hand</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>M05.351</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of right hip</td>
</tr>
<tr>
<td>M05.352</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of left hip</td>
</tr>
<tr>
<td>M05.359</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified hip</td>
</tr>
<tr>
<td>M05.361</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of right knee</td>
</tr>
<tr>
<td>M05.362</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of left knee</td>
</tr>
<tr>
<td>M05.369</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified knee</td>
</tr>
<tr>
<td>M05.371</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot</td>
</tr>
<tr>
<td>M05.372</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot</td>
</tr>
<tr>
<td>M05.379</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of unspecified ankle and foot</td>
</tr>
<tr>
<td>M05.39</td>
<td>Rheumatoid heart disease with rheumatoid arthritis of multiple sites</td>
</tr>
<tr>
<td>M05.40</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified site</td>
</tr>
<tr>
<td>M05.411</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of right shoulder</td>
</tr>
<tr>
<td>M05.412</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of left shoulder</td>
</tr>
<tr>
<td>M05.419</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified shoulder</td>
</tr>
<tr>
<td>M05.421</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of right elbow</td>
</tr>
<tr>
<td>M05.422</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of left elbow</td>
</tr>
<tr>
<td>M05.429</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified elbow</td>
</tr>
<tr>
<td>M05.431</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of right wrist</td>
</tr>
<tr>
<td>M05.432</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of left wrist</td>
</tr>
<tr>
<td>M05.439</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified wrist</td>
</tr>
<tr>
<td>M05.441</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of right hand</td>
</tr>
<tr>
<td>M05.442</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of left hand</td>
</tr>
<tr>
<td>M05.449</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified hand</td>
</tr>
<tr>
<td>M05.451</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of right hip</td>
</tr>
<tr>
<td>M05.452</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of left hip</td>
</tr>
<tr>
<td>M05.459</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified hip</td>
</tr>
<tr>
<td>M05.461</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of right knee</td>
</tr>
<tr>
<td>M05.462</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of left knee</td>
</tr>
<tr>
<td>M05.469</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified knee</td>
</tr>
<tr>
<td>M05.471</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot</td>
</tr>
<tr>
<td>M05.472</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot</td>
</tr>
<tr>
<td>M05.479</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of unspecified ankle and foot</td>
</tr>
<tr>
<td>M05.49</td>
<td>Rheumatoid myopathy with rheumatoid arthritis of multiple sites</td>
</tr>
<tr>
<td>M05.50</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site</td>
</tr>
<tr>
<td>M05.511</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder</td>
</tr>
<tr>
<td>M05.512</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder</td>
</tr>
<tr>
<td>M05.519</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified shoulder</td>
</tr>
<tr>
<td>M05.521</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow</td>
</tr>
<tr>
<td>M05.522</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow</td>
</tr>
<tr>
<td>M05.529</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified elbow</td>
</tr>
<tr>
<td>M05.531</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist</td>
</tr>
<tr>
<td>M05.532</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>M05.539</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified wrist</td>
</tr>
<tr>
<td>M05.541</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of right hand</td>
</tr>
<tr>
<td>M05.542</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of left hand</td>
</tr>
<tr>
<td>M05.549</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hand</td>
</tr>
<tr>
<td>M05.551</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of right hip</td>
</tr>
<tr>
<td>M05.552</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of left hip</td>
</tr>
<tr>
<td>M05.559</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified hip</td>
</tr>
<tr>
<td>M05.561</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of right knee</td>
</tr>
<tr>
<td>M05.562</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of left knee</td>
</tr>
<tr>
<td>M05.569</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified knee</td>
</tr>
<tr>
<td>M05.571</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot</td>
</tr>
<tr>
<td>M05.572</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot</td>
</tr>
<tr>
<td>M05.579</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified ankle and foot</td>
</tr>
<tr>
<td>M05.59</td>
<td>Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites</td>
</tr>
<tr>
<td>M05.60</td>
<td>Rheumatoid arthritis of unspecified site with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.611</td>
<td>Rheumatoid arthritis of right shoulder with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.612</td>
<td>Rheumatoid arthritis of left shoulder with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.619</td>
<td>Rheumatoid arthritis of unspecified shoulder with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.621</td>
<td>Rheumatoid arthritis of right elbow with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.622</td>
<td>Rheumatoid arthritis of left elbow with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.629</td>
<td>Rheumatoid arthritis of unspecified elbow with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.631</td>
<td>Rheumatoid arthritis of right wrist with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.632</td>
<td>Rheumatoid arthritis of left wrist with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.639</td>
<td>Rheumatoid arthritis of unspecified wrist with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.641</td>
<td>Rheumatoid arthritis of right hand with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.642</td>
<td>Rheumatoid arthritis of left hand with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.649</td>
<td>Rheumatoid arthritis of unspecified hand with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.651</td>
<td>Rheumatoid arthritis of right hip with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.652</td>
<td>Rheumatoid arthritis of left hip with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.659</td>
<td>Rheumatoid arthritis of unspecified hip with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.661</td>
<td>Rheumatoid arthritis of right knee with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.662</td>
<td>Rheumatoid arthritis of left knee with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.669</td>
<td>Rheumatoid arthritis of unspecified knee with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.671</td>
<td>Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.672</td>
<td>Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.679</td>
<td>Rheumatoid arthritis of unspecified ankle and foot with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.69</td>
<td>Rheumatoid arthritis of multiple sites with involvement of other organs and systems</td>
</tr>
<tr>
<td>M05.70</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement</td>
</tr>
<tr>
<td>M05.711</td>
<td>Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement</td>
</tr>
<tr>
<td>M05.712</td>
<td>Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement</td>
</tr>
<tr>
<td>M05.719</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified shoulder without organ or systems involvement</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>M05.721</td>
<td>Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement</td>
</tr>
<tr>
<td>M05.722</td>
<td>Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement</td>
</tr>
<tr>
<td>M05.729</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified elbow without organ or systems involvement</td>
</tr>
<tr>
<td>M05.731</td>
<td>Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement</td>
</tr>
<tr>
<td>M05.732</td>
<td>Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement</td>
</tr>
<tr>
<td>M05.739</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified wrist without organ or systems involvement</td>
</tr>
<tr>
<td>M05.741</td>
<td>Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement</td>
</tr>
<tr>
<td>M05.742</td>
<td>Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement</td>
</tr>
<tr>
<td>M05.749</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified hand without organ or systems involvement</td>
</tr>
<tr>
<td>M05.751</td>
<td>Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement</td>
</tr>
<tr>
<td>M05.752</td>
<td>Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement</td>
</tr>
<tr>
<td>M05.759</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified hip without organ or systems involvement</td>
</tr>
<tr>
<td>M05.761</td>
<td>Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement</td>
</tr>
<tr>
<td>M05.762</td>
<td>Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement</td>
</tr>
<tr>
<td>M05.769</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified knee without organ or systems involvement</td>
</tr>
<tr>
<td>M05.771</td>
<td>Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement</td>
</tr>
<tr>
<td>M05.772</td>
<td>Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement</td>
</tr>
<tr>
<td>M05.779</td>
<td>Rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot without organ or systems involvement</td>
</tr>
<tr>
<td>M05.79</td>
<td>Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement</td>
</tr>
<tr>
<td>M05.7A</td>
<td>Rheumatoid arthritis with rheumatoid factor of other specified site without organ or systems involvement</td>
</tr>
<tr>
<td>M05.80</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified site</td>
</tr>
<tr>
<td>M05.811</td>
<td>Other rheumatoid arthritis with rheumatoid factor of right shoulder</td>
</tr>
<tr>
<td>M05.812</td>
<td>Other rheumatoid arthritis with rheumatoid factor of left shoulder</td>
</tr>
<tr>
<td>M05.819</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified shoulder</td>
</tr>
<tr>
<td>M05.821</td>
<td>Other rheumatoid arthritis with rheumatoid factor of right elbow</td>
</tr>
<tr>
<td>M05.822</td>
<td>Other rheumatoid arthritis with rheumatoid factor of left elbow</td>
</tr>
<tr>
<td>M05.829</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified elbow</td>
</tr>
<tr>
<td>M05.831</td>
<td>Other rheumatoid arthritis with rheumatoid factor of right wrist</td>
</tr>
<tr>
<td>M05.832</td>
<td>Other rheumatoid arthritis with rheumatoid factor of left wrist</td>
</tr>
<tr>
<td>M05.839</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified wrist</td>
</tr>
<tr>
<td>M05.841</td>
<td>Other rheumatoid arthritis with rheumatoid factor of right hand</td>
</tr>
<tr>
<td>M05.842</td>
<td>Other rheumatoid arthritis with rheumatoid factor of left hand</td>
</tr>
<tr>
<td>M05.849</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified hand</td>
</tr>
<tr>
<td>M05.851</td>
<td>Other rheumatoid arthritis with rheumatoid factor of right hip</td>
</tr>
<tr>
<td>M05.852</td>
<td>Other rheumatoid arthritis with rheumatoid factor of left hip</td>
</tr>
<tr>
<td>M05.859</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified hip</td>
</tr>
<tr>
<td>M05.861</td>
<td>Other rheumatoid arthritis with rheumatoid factor of right knee</td>
</tr>
<tr>
<td>M05.862</td>
<td>Other rheumatoid arthritis with rheumatoid factor of left knee</td>
</tr>
<tr>
<td>M05.869</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified knee</td>
</tr>
<tr>
<td>M05.871</td>
<td>Other rheumatoid arthritis with rheumatoid factor of right ankle and foot</td>
</tr>
<tr>
<td>M05.872</td>
<td>Other rheumatoid arthritis with rheumatoid factor of left ankle and foot</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------</td>
</tr>
<tr>
<td>M05.879</td>
<td>Other rheumatoid arthritis with rheumatoid factor of unspecified ankle and foot</td>
</tr>
<tr>
<td>M05.89</td>
<td>Other rheumatoid arthritis with rheumatoid factor of multiple sites</td>
</tr>
<tr>
<td>M05.8A</td>
<td>Other rheumatoid arthritis with rheumatoid factor of other specified site</td>
</tr>
<tr>
<td>M05.9</td>
<td>Rheumatoid arthritis with rheumatoid factor, unspecified</td>
</tr>
<tr>
<td>M06.00</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified site</td>
</tr>
<tr>
<td>M06.011</td>
<td>Rheumatoid arthritis without rheumatoid factor, right shoulder</td>
</tr>
<tr>
<td>M06.012</td>
<td>Rheumatoid arthritis without rheumatoid factor, left shoulder</td>
</tr>
<tr>
<td>M06.019</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified shoulder</td>
</tr>
<tr>
<td>M06.021</td>
<td>Rheumatoid arthritis without rheumatoid factor, right elbow</td>
</tr>
<tr>
<td>M06.022</td>
<td>Rheumatoid arthritis without rheumatoid factor, left elbow</td>
</tr>
<tr>
<td>M06.029</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified elbow</td>
</tr>
<tr>
<td>M06.031</td>
<td>Rheumatoid arthritis without rheumatoid factor, right wrist</td>
</tr>
<tr>
<td>M06.032</td>
<td>Rheumatoid arthritis without rheumatoid factor, left wrist</td>
</tr>
<tr>
<td>M06.039</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified wrist</td>
</tr>
<tr>
<td>M06.041</td>
<td>Rheumatoid arthritis without rheumatoid factor, right hand</td>
</tr>
<tr>
<td>M06.042</td>
<td>Rheumatoid arthritis without rheumatoid factor, left hand</td>
</tr>
<tr>
<td>M06.049</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified hand</td>
</tr>
<tr>
<td>M06.051</td>
<td>Rheumatoid arthritis without rheumatoid factor, right hip</td>
</tr>
<tr>
<td>M06.052</td>
<td>Rheumatoid arthritis without rheumatoid factor, left hip</td>
</tr>
<tr>
<td>M06.059</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified hip</td>
</tr>
<tr>
<td>M06.061</td>
<td>Rheumatoid arthritis without rheumatoid factor, right knee</td>
</tr>
<tr>
<td>M06.062</td>
<td>Rheumatoid arthritis without rheumatoid factor, left knee</td>
</tr>
<tr>
<td>M06.069</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified knee</td>
</tr>
<tr>
<td>M06.071</td>
<td>Rheumatoid arthritis without rheumatoid factor, right ankle and foot</td>
</tr>
<tr>
<td>M06.072</td>
<td>Rheumatoid arthritis without rheumatoid factor, left ankle and foot</td>
</tr>
<tr>
<td>M06.079</td>
<td>Rheumatoid arthritis without rheumatoid factor, unspecified ankle and foot</td>
</tr>
<tr>
<td>M06.08</td>
<td>Rheumatoid arthritis without rheumatoid factor, vertebrae</td>
</tr>
<tr>
<td>M06.09</td>
<td>Rheumatoid arthritis without rheumatoid factor, multiple sites</td>
</tr>
<tr>
<td>M06.0A</td>
<td>Rheumatoid arthritis without rheumatoid factor, other specified site</td>
</tr>
<tr>
<td>M06.1</td>
<td>Adult-onset Still’s disease</td>
</tr>
<tr>
<td>M06.20</td>
<td>Rheumatoid bursitis, unspecified site</td>
</tr>
<tr>
<td>M06.211</td>
<td>Rheumatoid bursitis, right shoulder</td>
</tr>
<tr>
<td>M06.212</td>
<td>Rheumatoid bursitis, left shoulder</td>
</tr>
<tr>
<td>M06.219</td>
<td>Rheumatoid bursitis, unspecified shoulder</td>
</tr>
<tr>
<td>M06.221</td>
<td>Rheumatoid bursitis, right elbow</td>
</tr>
<tr>
<td>M06.222</td>
<td>Rheumatoid bursitis, left elbow</td>
</tr>
<tr>
<td>M06.229</td>
<td>Rheumatoid bursitis, unspecified elbow</td>
</tr>
<tr>
<td>M06.231</td>
<td>Rheumatoid bursitis, right wrist</td>
</tr>
<tr>
<td>M06.232</td>
<td>Rheumatoid bursitis, left wrist</td>
</tr>
<tr>
<td>M06.239</td>
<td>Rheumatoid bursitis, unspecified wrist</td>
</tr>
<tr>
<td>M06.241</td>
<td>Rheumatoid bursitis, right hand</td>
</tr>
<tr>
<td>M06.242</td>
<td>Rheumatoid bursitis, left hand</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>---------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>M06.249</td>
<td>Rheumatoid bursitis, unspecified hand</td>
</tr>
<tr>
<td>M06.251</td>
<td>Rheumatoid bursitis, right hip</td>
</tr>
<tr>
<td>M06.252</td>
<td>Rheumatoid bursitis, left hip</td>
</tr>
<tr>
<td>M06.259</td>
<td>Rheumatoid bursitis, unspecified hip</td>
</tr>
<tr>
<td>M06.261</td>
<td>Rheumatoid bursitis, right knee</td>
</tr>
<tr>
<td>M06.262</td>
<td>Rheumatoid bursitis, left knee</td>
</tr>
<tr>
<td>M06.269</td>
<td>Rheumatoid bursitis, unspecified knee</td>
</tr>
<tr>
<td>M06.271</td>
<td>Rheumatoid bursitis, right ankle and foot</td>
</tr>
<tr>
<td>M06.272</td>
<td>Rheumatoid bursitis, left ankle and foot</td>
</tr>
<tr>
<td>M06.279</td>
<td>Rheumatoid bursitis, unspecified ankle and foot</td>
</tr>
<tr>
<td>M06.28</td>
<td>Rheumatoid bursitis, vertebrae</td>
</tr>
<tr>
<td>M06.29</td>
<td>Rheumatoid bursitis, multiple sites</td>
</tr>
<tr>
<td>M06.30</td>
<td>Rheumatoid nodule, unspecified site</td>
</tr>
<tr>
<td>M06.311</td>
<td>Rheumatoid nodule, right shoulder</td>
</tr>
<tr>
<td>M06.312</td>
<td>Rheumatoid nodule, left shoulder</td>
</tr>
<tr>
<td>M06.319</td>
<td>Rheumatoid nodule, unspecified shoulder</td>
</tr>
<tr>
<td>M06.321</td>
<td>Rheumatoid nodule, right elbow</td>
</tr>
<tr>
<td>M06.322</td>
<td>Rheumatoid nodule, left elbow</td>
</tr>
<tr>
<td>M06.329</td>
<td>Rheumatoid nodule, unspecified elbow</td>
</tr>
<tr>
<td>M06.331</td>
<td>Rheumatoid nodule, right wrist</td>
</tr>
<tr>
<td>M06.332</td>
<td>Rheumatoid nodule, left wrist</td>
</tr>
<tr>
<td>M06.339</td>
<td>Rheumatoid nodule, unspecified wrist</td>
</tr>
<tr>
<td>M06.341</td>
<td>Rheumatoid nodule, right hand</td>
</tr>
<tr>
<td>M06.342</td>
<td>Rheumatoid nodule, left hand</td>
</tr>
<tr>
<td>M06.349</td>
<td>Rheumatoid nodule, unspecified hand</td>
</tr>
<tr>
<td>M06.351</td>
<td>Rheumatoid nodule, right hip</td>
</tr>
<tr>
<td>M06.352</td>
<td>Rheumatoid nodule, left hip</td>
</tr>
<tr>
<td>M06.359</td>
<td>Rheumatoid nodule, unspecified hip</td>
</tr>
<tr>
<td>M06.361</td>
<td>Rheumatoid nodule, right knee</td>
</tr>
<tr>
<td>M06.362</td>
<td>Rheumatoid nodule, left knee</td>
</tr>
<tr>
<td>M06.369</td>
<td>Rheumatoid nodule, unspecified knee</td>
</tr>
<tr>
<td>M06.371</td>
<td>Rheumatoid nodule, right ankle and foot</td>
</tr>
<tr>
<td>M06.372</td>
<td>Rheumatoid nodule, left ankle and foot</td>
</tr>
<tr>
<td>M06.379</td>
<td>Rheumatoid nodule, unspecified ankle and foot</td>
</tr>
<tr>
<td>M06.38</td>
<td>Rheumatoid nodule, vertebrae</td>
</tr>
<tr>
<td>M06.39</td>
<td>Rheumatoid nodule, multiple sites</td>
</tr>
<tr>
<td>M06.4</td>
<td>Inflammatory polyarthropathy</td>
</tr>
<tr>
<td>M06.80</td>
<td>Other specified rheumatoid arthritis, unspecified site</td>
</tr>
<tr>
<td>M06.811</td>
<td>Other specified rheumatoid arthritis, right shoulder</td>
</tr>
<tr>
<td>M06.812</td>
<td>Other specified rheumatoid arthritis, left shoulder</td>
</tr>
<tr>
<td>M06.819</td>
<td>Other specified rheumatoid arthritis, unspecified shoulder</td>
</tr>
<tr>
<td>M06.821</td>
<td>Other specified rheumatoid arthritis, right elbow</td>
</tr>
<tr>
<td>Diagnosis Code</td>
<td>Description</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>M06.822</td>
<td>Other specified rheumatoid arthritis, left elbow</td>
</tr>
<tr>
<td>M06.829</td>
<td>Other specified rheumatoid arthritis, unspecified elbow</td>
</tr>
<tr>
<td>M06.831</td>
<td>Other specified rheumatoid arthritis, right wrist</td>
</tr>
<tr>
<td>M06.832</td>
<td>Other specified rheumatoid arthritis, left wrist</td>
</tr>
<tr>
<td>M06.839</td>
<td>Other specified rheumatoid arthritis, unspecified wrist</td>
</tr>
<tr>
<td>M06.841</td>
<td>Other specified rheumatoid arthritis, right hand</td>
</tr>
<tr>
<td>M06.842</td>
<td>Other specified rheumatoid arthritis, left hand</td>
</tr>
<tr>
<td>M06.849</td>
<td>Other specified rheumatoid arthritis, unspecified hand</td>
</tr>
<tr>
<td>M06.851</td>
<td>Other specified rheumatoid arthritis, right hip</td>
</tr>
<tr>
<td>M06.852</td>
<td>Other specified rheumatoid arthritis, left hip</td>
</tr>
<tr>
<td>M06.859</td>
<td>Other specified rheumatoid arthritis, unspecified hip</td>
</tr>
<tr>
<td>M06.861</td>
<td>Other specified rheumatoid arthritis, right knee</td>
</tr>
<tr>
<td>M06.862</td>
<td>Other specified rheumatoid arthritis, left knee</td>
</tr>
<tr>
<td>M06.869</td>
<td>Other specified rheumatoid arthritis, unspecified knee</td>
</tr>
<tr>
<td>M06.871</td>
<td>Other specified rheumatoid arthritis, right ankle and foot</td>
</tr>
<tr>
<td>M06.872</td>
<td>Other specified rheumatoid arthritis, left ankle and foot</td>
</tr>
<tr>
<td>M06.879</td>
<td>Other specified rheumatoid arthritis, unspecified ankle and foot</td>
</tr>
<tr>
<td>M06.88</td>
<td>Other specified rheumatoid arthritis, vertebrae</td>
</tr>
<tr>
<td>M06.89</td>
<td>Other specified rheumatoid arthritis, multiple sites</td>
</tr>
<tr>
<td>M06.8A</td>
<td>Other specified rheumatoid arthritis, other specified site</td>
</tr>
<tr>
<td>M06.9</td>
<td>Rheumatoid arthritis, unspecified</td>
</tr>
<tr>
<td>M08.1</td>
<td>Juvenile ankylosing spondylitis</td>
</tr>
<tr>
<td>M45.0</td>
<td>Ankylosing spondylitis of multiple sites in spine</td>
</tr>
<tr>
<td>M45.1</td>
<td>Ankylosing spondylitis of occipito-atlanto-axial region</td>
</tr>
<tr>
<td>M45.2</td>
<td>Ankylosing spondylitis of cervical region</td>
</tr>
<tr>
<td>M45.3</td>
<td>Ankylosing spondylitis of cervicothoracic region</td>
</tr>
<tr>
<td>M45.4</td>
<td>Ankylosing spondylitis of thoracic region</td>
</tr>
<tr>
<td>M45.5</td>
<td>Ankylosing spondylitis of thoracolumbar region</td>
</tr>
<tr>
<td>M45.6</td>
<td>Ankylosing spondylitis lumbar region</td>
</tr>
<tr>
<td>M45.7</td>
<td>Ankylosing spondylitis of lumbosacral region</td>
</tr>
<tr>
<td>M45.8</td>
<td>Ankylosing spondylitis sacral and sacrococcygeal region</td>
</tr>
<tr>
<td>M45.9</td>
<td>Ankylosing spondylitis of unspecified sites in spine</td>
</tr>
<tr>
<td>M48.8X1</td>
<td>Other specified spondylopathies, occipito-atlanto-axial region</td>
</tr>
<tr>
<td>M48.8X2</td>
<td>Other specified spondylopathies, cervical region</td>
</tr>
<tr>
<td>M48.8X3</td>
<td>Other specified spondylopathies, cervicothoracic region</td>
</tr>
<tr>
<td>M48.8X4</td>
<td>Other specified spondylopathies, thoracic region</td>
</tr>
<tr>
<td>M48.8X5</td>
<td>Other specified spondylopathies, thoracolumbar region</td>
</tr>
<tr>
<td>M48.8X6</td>
<td>Other specified spondylopathies, lumbar region</td>
</tr>
<tr>
<td>M48.8X7</td>
<td>Other specified spondylopathies, lumbosacral region</td>
</tr>
<tr>
<td>M48.8X8</td>
<td>Other specified spondylopathies, sacral and sacrococcygeal region</td>
</tr>
<tr>
<td>M48.8X9</td>
<td>Other specified spondylopathies, site unspecified</td>
</tr>
<tr>
<td>N17.8</td>
<td>Other acute kidney failure</td>
</tr>
</tbody>
</table>
### Background

Infliximab is a genetically engineered chimeric human/mouse monoclonal antibody (cA2) against tumor necrosis factor alfa (TNF-alfa), 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. TNF-alfa activity is neutralized by cA2 antibody binding to the soluble and transmembrane forms which blocks the binding of TNF-alfa with its receptors. Activities inhibited by anti-TNF-alfa antibodies include induction of interleukins, enhancement of leukocyte migration, and expression of adhesion molecules. In vitro studies have demonstrated that cells expressing transmembrane TNF-alfa bound by infliximab are lysed by complement or effector cells. In animal models, antibodies to TNF-alfa were shown to prevent or reduce inflammation.1

### Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. See the Policy and Procedure addressing the treatment of serious rare diseases.

### Clinical Evidence

#### Proven

**Sarcoidosis**

The use of infliximab in patients with chronic pulmonary sarcoidosis was assessed in a multicenter, randomized, double-blind, placebo-controlled study.52 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).

Infliximab has also been studied for use in sarcoidosis in small clinical trials, small published studies and reports that also conclude that clinical evidence supports the use of infliximab for treatment-resistant sarcoidosis.6,25,39,40,46

**Noninfectious Uveitis**

Long-term safety and efficacy of treatment with infliximab in uveitis for more than one year in patients (n=164) with Behçet’s disease (BD) was evaluated via questionnaire in a retrospective multicenter study.12 Primary outcome measures assessed were best-corrected VA (BCVA) determined by the Landolt ring, proportion of subjects without relapse of uveitis, frequency of ocular

---

**Table:**

<table>
<thead>
<tr>
<th>Diagnosis Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N17.9</td>
<td>Acute kidney failure, unspecified</td>
</tr>
<tr>
<td>N82.2</td>
<td>Fistula of vagina to small intestine</td>
</tr>
<tr>
<td>N82.3</td>
<td>Fistula of vagina to large intestine</td>
</tr>
<tr>
<td>N82.4</td>
<td>Other female intestinal-genital tract fistulae</td>
</tr>
<tr>
<td>R19.7</td>
<td>Diarrhea, unspecified</td>
</tr>
<tr>
<td>T45.1X5A</td>
<td>Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter</td>
</tr>
<tr>
<td>T45.1X5D</td>
<td>Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter</td>
</tr>
<tr>
<td>T45.1X5S</td>
<td>Adverse effect of antineoplastic and immunosuppressive drugs, sequela</td>
</tr>
</tbody>
</table>

---

UnitedHealthcare Commercial Medical Benefit Drug Policy

Proprietary Information of UnitedHealthcare. Copyright 2022 United HealthCare Services, Inc.

Effective 03/01/2022
Inflammatory attacks per year, and adverse effects of the therapy. The mean age at initiation of infliximab treatment was 42.6±11.7 years, and the mean treatment duration was 32.9±14.4 months. Data before and at the last visit during infliximab treatment were analyzed in 4 groups divided by duration of treatment: group A (n=43, 12-<24 months), group B (n=62, 24-<36 months), group C (n=42, 36-<48 months), and group D (n=17, ≥48 months). The frequency of ocular attacks decreased in all groups (from 5.3±3.0 to 1.0±0.3 in group A, 4.8±4.6 to 1.4±0.3 in group B, 4.1±2.9 to 0.9±0.3 in group C, and 9.5±5.8 to 1.6±0.5 in group D; all P < 0.05). The BCVA was improved in approximately 55% of the eyes after treatment. Mean BCVA was improved after treatment with infliximab in groups A to C (from 0.79±1.04 to 0.59±0.94 in group A, 0.59±1.07 to 0.41±1.04 in group B, and 1.15±1.77 to 0.92±1.73 in group C; all P < 0.05) but not in group D. Uveitis relapsed in 59.1% of all patients after infliximab treatment, and no difference in duration until relapse was observed between individual groups. Approximately 80% of relapses occurred within one year after the initiation of infliximab treatment in all groups, 90% of which were controlled by increasing doses of topical corticosteroids and shortening the interval of infliximab infusion. Adverse effects were observed in 65 cases or 35% of all subjects. Infliximab treatment was continued in 85% of the patients, but 15% of the patients discontinued infliximab treatment because of adverse effects or insufficient efficacy. Researchers concluded that this study demonstrated that infliximab reduced the frequency of ocular attacks and improved VA in patients with BD-related uveitis refractory to conventional therapies and was generally well tolerated, with few serious adverse events.

Kruh et al conducted a retrospective, interventional, non-comparative cohort study which evaluated the safety and efficacy of infliximab for the treatment of refractory noninfectious uveitis. Patients (n=88) with chronic, recalcitrant uveitis treated with infliximab were identified through an electronic medical record database. All charts were reviewed for sex, diagnosis, location of inflammation, presence of vasculitis, prior immunomodulatory treatments, duration of infliximab treatment, dose received, secondary side effects, and other medications continued while receiving treatment with infliximab. The primary outcome measures assessed were the rate of remission, time to remission, relapse rate, failure rate, and patient tolerance. Additional analysis was aimed to identify risk factors that would predict a higher success rate of infliximab to treat various types of noninfectious uveitis. Of the 72 patients (81.8%) who achieved clinical remission while being treated with infliximab, 42 (58.3%) required additional immunomodulatory medications. At 7, 18.1, and 44.7 weeks, 25%, 50%, and 75% of patients, respectively, achieved clinical remission off all corticosteroids. Thirty-two patients (36.4%) experienced at least one side effect while on infliximab therapy, and 17 patients (19.3%) discontinued infliximab treatment secondary to one or more intolerable side effects. The most common adverse effects were skin rash (9.1%) and fatigue (8%). Factors associated with a higher chance to achieve clinical remission were non-idiopathic uveitis (P < 0.011), intermediate or panuveitis (P < 0.001), absence of vasculitis (P < 0.001), and a starting dose ≥5 mg/kg (P < 0.011). Researchers concluded that infliximab treatment induced a high rate of complete clinical remission in recalcitrant uveitis and is well tolerated by most patients.

**NCCN Recommended Uses**

According to the NCCN Drugs & Biologics Compendium, NCCN recommends (2A) infliximab for the treatment of:

- Acute graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.
  - Therapy for steroid-refractory acute GVHD is often used in conjunction with the original immunosuppressive agent
- Immune checkpoint inhibitor-related toxicities - Consider adding infliximab for the management of immunotherapy-related:
  - Moderate (G2) and strongly consider for severe (G3-4) diarrhea or colitis if no response after 2 days of systemic corticosteroids
  - Severe (G3-4) pneumonitis if no improvement after 2 days of systemic corticosteroids
  - Severe (G3) or life-threatening (G4) acute renal failure/elevated serum creatinine if toxicity remains >G2 after 1 week of systemic corticosteroids
  - G3-4 uveitis that is refractory to high-dose systemic corticosteroids
  - Severe (G3) or life-threatening (G4) myocarditis, pericarditis, arrhythmias, impaired ventricular function, or conduction abnormalities if no improvement within 24 hours of starting pulse-dose methylprednisolone
  - Severe inflammatory arthritis as additional disease modifying anti-rheumatic therapy if symptoms do not improve after 7 days of starting high-dose corticosteroids
  - Moderate, severe, or life-threatening steroid-refractory myalgias or myositis if refractory to steroids

**Unproven**

**Juvenile Idiopathic Arthritis (Juvenile Rheumatoid Arthritis)**

In an international, multicenter, randomized, placebo-controlled, double-blind study, 122 children with polyarticular juvenile rheumatoid arthritis (JRA) and persistent symptoms despite at least 3 months prior MTX were randomized to receive infliximab...
3 mg/kg + MTX or placebo + MTX at weeks 0, 2, and 6. At week 14, the placebo group was switched to infliximab 6 mg/kg + placebo. Responses were measured according to American College of Rheumatology Pediatric 30 (Pedi 30) criteria. Although a higher percentage of patients in the 3 mg/kg group achieved responses at week 14 (63.8% vs. 49.2% in placebo group), the study failed to show the efficacy of infliximab for JRA as the difference was not statistically significant. By week 16, similar percentage response was achieved in both groups. At week 52, the percentages reaching ACR Pedi 50 and ACR Pedi 70 were 69.6% and 51.8%, respectively. The safety profile of infliximab 3 mg/kg was generally less favorable than that of infliximab 6 mg/kg, with more serious adverse events, infusion reactions, antibodies to infliximab, and newly induced antinuclear antibodies and antibodies to double-stranded DNA. Patients who completed the study also continued to receive open-label treatment for up to 2 years.

Infliximab has also been studied for use in JIA in smaller, open-label trials. Further large scale studies are required to characterize the efficacy and safety of infliximab in JIA.

**Miscellaneous**

The medical literature contains a number of small open-label studies and case reports of infliximab therapy for the treatment of adult-onset Still’s disease, Sjögren’s syndrome, myelodysplastic syndromes, undifferentiated spondyloarthropathy, Reiter’s syndrome, hidradenitis suppurativa, and Wegener’s granulomatosis. While these studies and reports showed infliximab to have a positive effect on the manifestations of these diseases, the use of infliximab for these conditions has not been evaluated in large, controlled trials.

**Professional Societies**

**Ulcerative Colitis**

In 2020, the American Gastroenterological Association (AGA) published a clinical practice guideline on the management of moderate to severe ulcerative colitis. In regard to infliximab, the guidelines recommend:

- In adult outpatients with moderate-severe ulcerative colitis, the AGA recommends using infliximab, adalimumab, golimumab, vedolizumab, tofacitinib or ustekinumab over no treatment. (Strong recommendation, moderate quality evidence)
- In adult outpatients with moderate-severe ulcerative colitis who are naïve to biologic agents, the AGA suggests using infliximab or vedolizumab rather than adalimumab, for induction of remission. (Conditional recommendation, moderate quality evidence)
- In adult outpatients with moderate-severe ulcerative colitis who have previously been exposed to infliximab, particularly those with primary non-response, the AGA suggests using ustekinumab or tofacitinib, rather than vedolizumab or adalimumab for induction of remission. (Conditional recommendation, low quality evidence)
- In adult outpatients with active moderate-severe ulcerative colitis, the AGA suggests using biologic monotherapy (TNFα antagonists, vedolizumab, ustekinumab) rather than thiopurine monotherapy for induction of remission. (Conditional recommendation, low quality evidence)
- In adult outpatients with moderate-severe ulcerative colitis in remission, the AGA makes no recommendation in favor of, or against, using biologic monotherapy (TNFα antagonists, vedolizumab or ustekinumab), rather than thiopurine monotherapy for maintenance of remission. (No recommendation, knowledge gap)
- In adult outpatients with moderate-severe ulcerative colitis, the AGA suggests combining TNFα antagonists, vedolizumab or ustekinumab with thiopurines or methotrexate, rather than biologic monotherapy. (Conditional recommendation, low quality evidence)
- In adult outpatients with moderate-severe ulcerative colitis, the AGA suggests using thiopurines or methotrexate, rather than biologic monotherapy. (Conditional recommendation, low quality evidence)
- In adult outpatients with moderate-severe ulcerative colitis, the AGA suggests early use of biologic agents with or without immunomodulator therapy, rather than gradual step up after failure of 5-aminosalicylates. (Conditional recommendation, very low-quality evidence)
- In adult outpatients with moderate-severe ulcerative colitis who have achieved remission with biologic agents and/or immunomodulators, or tofacitinib, the AGA suggests against continuing 5-aminosalicylates for induction and maintenance of remission. (Conditional recommendation, very low-quality evidence)
- In hospitalized adult patients with acute severe ulcerative colitis refractory to intravenous corticosteroids, the AGA suggests using infliximab or cyclosporine. (Conditional recommendation, low quality evidence)
In hospitalized adult patients with acute severe ulcerative colitis, refractory to intravenous corticosteroids, being treated with infliximab, the AGA makes no recommendation on routine use of intensive vs. standard infliximab dosing. (No recommendation, knowledge gap)

The American College of Gastroenterology (ACG) published their guidelines for the management of adults with ulcerative colitis in 2019. In regard to infliximab or anti-TNF therapy, the guidelines recommend:

### Summary and strength of graded recommendations for the management of ulcerative colitis

- **Induction of remission in moderately to severely active ulcerative colitis**
  - In patients with moderately to severely active UC, the ACG recommends anti-TNF therapy using adalimumab, golimumab, or infliximab for induction of remission (strong recommendation, high quality of evidence).
  - In patients with moderately to severely active UC who have failed 5-ASA therapy and in whom anti-TNF therapy is used for induction of remission, the ACG suggests against using 5-ASA for added clinical efficacy (conditional recommendation, low quality of evidence).
  - When infliximab is used as induction therapy for patients with moderately to severely active UC, the ACG recommends combination therapy with a thiouprine (strong recommendation, moderate quality of evidence for azathioprine).

- **Maintenance of remission in patients with previously moderately to severely active ulcerative colitis**
  - In patients with previously moderately to severely active UC who have achieved remission but previously failed 5-ASA therapy and are now on anti-TNF therapy, the ACG recommends against using concomitant 5-ASA for efficacy of maintenance of remission (conditional recommendation, low quality of evidence).
  - The ACG recommends continuing anti-TNF therapy using adalimumab, golimumab, or infliximab to maintain remission after anti-TNF induction in patients with previously moderately to severely active UC (strong recommendation, moderate quality of evidence).

- **Management of the hospitalized patient with acute severe ulcerative colitis (ASUC)**
  - In patients with ASUC failing to adequately respond to intravenous corticosteroids by 3–5 days the ACG recommends medical rescue therapy with infliximab or cyclosporine (strong recommendation, moderate quality of evidence).
  - In patients with ASUC who achieve remission with infliximab treatment, the ACG recommends maintenance of remission with the same agent (strong recommendation, moderate quality of evidence).

### Summary of key concept statements for the management of ulcerative colitis

- **Induction of remission in moderately to severely active ulcerative colitis**
  - Robust data on combination anti-TNF and immunomodulator therapy in moderately to severely active UC exist only for infliximab and thiopurines.
  - Patients who are primary nonresponders to an anti-TNF (defined as lack of therapeutic benefit after induction despite adequate drug levels) should be evaluated and considered for alternative mechanisms of disease control (e.g., in a different class of therapy) rather than cycling to another drug within the anti-TNF class.
  - In patients with moderately to severely active UC who had an initial response but subsequently lost efficacy to one anti-TNF therapy, the ACG recommends alternative anti-TNF therapy (but not the biosimilar to the original brand) compared with no treatment for induction of remission.

---

**Plaque Psoriasis**

In 2019, the American Academy of Dermatology and the National Psoriasis Foundation published updated treatment guidelines for the management and treatment of psoriasis with biologic therapies. In regard to ustekinumab, the guidelines state:

- Infliximab is recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis
- The recommended starting dose of infliximab is an infusion of 5 mg/kg administered at week 0, week 2, and week 6, and thereafter it is administered every 8 weeks.
- Infliximab is recommended to be administered at a more frequent interval (less than every 8 weeks and as frequently as every 4 weeks during the maintenance phase) and/or at a higher dose up to 10 mg/kg for better disease control in some adult patients.
- Infliximab can be recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis affecting the palms and soles (plaque-type palmoplantar psoriasis).
- Infliximab can be recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis affecting the nails.
Infliximab can be recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis affecting the scalp.

Infliximab may be recommended as a monotherapy treatment option in adult patients with other subtypes (pustular or erythrodermic) of moderate-to-severe plaque psoriasis.

Infliximab is recommended as a monotherapy treatment option in adult patients with plaque psoriasis affecting the scalp.

Infliximab can be recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis affecting the scalp.

Infliximab is recommended as a monotherapy treatment option in adult patients with plaque psoriasis of any severity when associated with significant psoriatic arthritis. Infliximab also inhibits radiographically detected damage of joints in patients with psoriatic arthritis.

Combination of infliximab and topicals such as high-potency corticosteroids with or without a vitamin D analogue can be recommended as a treatment option to augment efficacy for the treatment of moderate-to-severe plaque psoriasis in adults.

Infliximab may be combined with acitretin to augment efficacy for the treatment of moderate-to-severe plaque psoriasis in adults.

Infliximab may be combined with methotrexate to possibly augment efficacy for the treatment of moderate-to-severe plaque psoriasis in adults.

Infliximab may be combined with apremilast to augment efficacy for the treatment of moderate-to-severe plaque psoriasis in adults when clinically indicated.

Psoriatic Arthritis

In 2018, the American College of Rheumatology and the National Psoriasis Foundation published treatment guidelines for the treatment of psoriatic arthritis. In regard to psoriatic arthritis (PsA) and TNFi’s, the guidelines state:

Recommendations for the initial treatment of patients with active psoriatic arthritis who are oral small molecule (OSM)-and other treatment-naïve patients:

- Treat with a TNFi biologic over an OSM:
  - Conditional recommendation based on low-quality evidence; may consider an OSM if the patient does not have severe PsA, does not have severe psoriasis, prefers oral therapy, has concern over starting a biologic as the first therapy, or has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

- Treat with a TNFi biologic over an IL-17i biologic
  - Conditional recommendation based on very-low-quality evidence; may consider an IL-17i biologic if the patient has severe psoriasis or has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

- Treat with a TNFi biologic over an IL-12/23i biologic
  - Conditional recommendation based on very-low-quality evidence; may consider an IL-12/23i biologic if the patient has severe psoriasis, prefers less frequent drug administration, or has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

Recommendations for treatment of patients with active psoriatic arthritis despite treatment with an OSM:

- Switch to a TNFi biologic over a different OSM
  - Conditional recommendation based on moderate-quality evidence; may consider switching to a different OSM if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, if the patient prefers oral versus parenteral therapy, or in patients without evidence of severe PsA or severe psoriasis.

- Switch to a TNFi biologic over an IL-17i biologic
  - Conditional recommendation based on moderate-quality evidence; may consider an IL-17i if the patient has severe psoriasis and/or has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, and/or a family history of demyelinating disease such as multiple sclerosis.

- Switch to a TNFi biologic over an IL-12/23i biologic
  - Conditional recommendation based on moderate-quality evidence; may consider an IL-12/23i if the patient has severe psoriasis and/or contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, or prefers less frequent drug administration.

- Switch to a TNFi biologic over abatacept
  - Conditional recommendation based on low-quality evidence; may consider abatacept if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

- Switch to a TNFi biologic over tofacitinib
• Conditional recommendation based on low-quality evidence; may consider tofacitinib if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, or prefers oral medication.
  o Switch to a TNFi biologic monotherapy over MTX and a TNFi biologic combination therapy
    • Conditional recommendation based on low-quality evidence; may consider MTX and TNFi biologic combination therapy if the patient has severe skin manifestations, has had a partial response to current MTX therapy, has concomitant uveitis (since uveitis may respond to MTX therapy), and if the current TNFi biologic is infliximab or adalimumab.

• Recommendations for treatment of patients with active psoriatic arthritis despite treatment with a TNFi biologic, as monotherapy or in combination with MTX
  o Switch to a different TNFi biologic over switching to an IL-17i biologic
    • Conditional recommendation based on low-quality evidence; may consider an IL-17i if the patient had a primary TNFi biologic efficacy failure or a TNFi biologic–associated serious adverse event or severe psoriasis.
  o Switch to a different TNFi biologic over switching to an IL-12/23i biologic
    • Conditional recommendation based on low-quality evidence; may consider an IL-12/23i if the patient had a primary TNFi biologic efficacy failure or a TNFi biologic–associated serious adverse event or prefers less frequent drug administration.
  o Switch to a different TNFi biologic over switching to abatacept
    • Conditional recommendation based on low-quality evidence; may consider abatacept if the patient had a primary TNFi biologic efficacy failure or TNFi biologic–associated serious adverse effect.
  o Switch to a different TNFi biologic over switching to tofacitinib
    • Conditional recommendation based on low-quality evidence; may consider tofacitinib if the patient prefers an oral therapy or had a primary TNFi biologic efficacy failure or a TNFi biologic–associated serious adverse effect.
  o Switch to a different TNFi biologic (with or without MTX) over adding MTX to the same TNFi biologic monotherapy
    • Conditional recommendation based on very-low-quality evidence; may consider adding MTX when patients have demonstrated partial response to the current TNFi biologic therapy, especially if the TNFi biologic is a monoclonal antibody.
  o Switch to a different TNFi biologic monotherapy over switching to a different TNFi biologic and MTX combination therapy
    • Conditional recommendation based on very-low-quality evidence; may consider switching to a TNFi biologic and MTX combination therapy if the current TNFi biologic is infliximab.

In adult patients with active PsA despite treatment with a TNFi biologic and MTX combination therapy,
  o Switch to a different TNFi biologic + MTX over switching to a different TNFi biologic monotherapy
    • Conditional recommendation based on very-low-quality evidence; may consider switching to a different TNFi biologic monotherapy if the patient has demonstrated MTX-associated adverse events, prefers to receive fewer medications, or perceives MTX as a burden.

**Ankylosing Spondylitis**

In 2017, the British Society for Rheumatology (BSR) and the British Health Professionals in Rheumatology published a revision to their 2005 BSR guidelines to provide guidance for clinicians in the United Kingdom prescribing biologic drugs for the treatment of axial spondyloarthritis (axSpA), including ankylosing spondylitis. This includes the criteria for starting treatment, choice of drug, and assessing response. In regard to tumor necrosis factor inhibitors (TNFi), the guidelines recommend:

• The effectiveness of biologics in axSpA:
  o Anti-TNF therapy is effective at reducing disease activity and spinal pain in axSpA. While short-term MRI data support the efficacy of anti-TNF therapy in treating inflammatory SIJ and spinal lesions in axSpA, evidence for anti-TNF therapy on radiographic disease progression is currently limited.
  o Currently there is insufficient evidence to recommend the use of other biologic agents in axSpA.

• Initiating treatment:
  o Patients should be considered for anti-TNF therapy if they have active axSpA

• Choice of Drug:
  o Extra-articular manifestations and patient choice should be considered when selecting an anti-TNF agent. In the absence of head-to-head studies, systematic reviews have shown no statistical difference in efficacy between infliximab, golimumab, etanercept and adalimumab in the treatment of AS (certolizumab data were not included in these comparative reviews, but its efficacy has been established in clinical trials).
There are insufficient data to comment on relative efficacy in nr-axSpA. However, not all biologics are licensed for or effective in the treatment of extra-articular disease, so drug choice should take into account co-morbidities and the preferred route and frequency of administration.

- **Assessing Response:**
  - Initial efficacy response should be assessed following 3–6 months of therapy and responders should then be reassessed every 6 months.

- **Withdrawal of Therapy:**
  - In the absence of an initial clinical response by 6 months, or failure to maintain response at two consecutive assessments, withdrawal of that anti-TNF agent should be considered.
  - There is no evidence to support the withdrawal of anti-TNF therapy in treatment responders.

- **Switching:**
  - In the event of anti-TNF failure due to inefficacy or adverse events, an alternative anti-TNF agent should be offered if clinically appropriate.

- **Safety:**
  - The safety of anti-TNF therapies in axSpA is comparable to other inflammatory joint diseases such as RA. There is little evidence to suggest that safety issues differ hugely with different disease groups, and the 2010 British Society for Rheumatology (BSR) guidelines on the safety of anti-TNF therapies in RA are applicable in axSpA.

In 2016, the Assessment of SpondyloArthritis international Society (ASAS) and European League Against Rheumatism (EULAR) updated and integrated the recommendations for ankylosing spondylitis (AS) and the recommendations for the use of tumor necrosis factor inhibitors (TNFi) in axial spondyloarthritis (axSpA) into one guideline applicable to the full spectrum of patients with axSpA. The recommendations describe all aspects of the management of patients with a diagnosis of axSpA. The recommendations related to biologic DMARDs (bDMARDs) are:

- bDMARDs should be considered in patients with persistently high disease activity despite conventional treatments (e.g., non-biologic DMARDs); current practice is to start with TNFi therapy.
- If TNFi therapy fails, switching to another TNFi or IL-17i therapy should be considered.
- If a patient is in sustained remission, tapering of a bDMARD can be considered.

**Crohn’s Disease**

According to the American College of Gastroenterology Practice Guidelines for the Management of Crohn’s Disease in Adults (ACG Practice Guidelines) published in February 2009, patients with moderate-severe disease usually have a Crohn’s Disease Activity Index (CDAI) of 220-450. They have failed to respond to treatment for mild-moderate disease, or have more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia.

The CDAI is the sum of the following clinical or laboratory variables after multiplying by their weighting factor given in parentheses:

- Number of liquid or soft stools each day for seven days (2)
- Abdominal pain graded from 0-3 in severity each day for seven days (5)
- General well-being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days (7)
- Presence of complications where 1 point is added for each complication (20). Complications include:
  - the presence of joint pains (arthralgia) or frank arthritis
  - inflammation of the iris or uveitis
  - presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers
  - anal fissures, fistulae or abscesses
  - other fistulae (e.g., enterocutaneous, vesicle, vaginal)
  - fever (>37.8°C) during the previous week
- Taking diphenoxylate/atropine [Lomotil®] or opiates for diarrhea (30)
- Presence of an abdominal mass where 0 = none, 2 = questionable, 5 = definite (10);
- Absolute deviation of hematocrit from 47% in males and 42% in females (6)
- Percentage deviation from standard body weight (1)
The 2018 ACG Practice Guidelines support the use of infliximab for treatment and maintenance of patients with moderate to severely active Crohn’s disease which is resistant or refractory to corticosteroids, thiopurines or methotrexate. In addition, they state anti-TNF agents can be considered to treat severely active Crohn’s disease.

**Rheumatoid Arthritis**

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDs, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (≥ 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs. The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions. Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

Supplementary Appendix 5, of the 2015 ACR RA guideline, summarizes recommendations for patients with early RA, established RA, and high-risk comorbidities:

**Recommendations for Early RA Patients**

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, another target may be chosen because risk tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with early, symptomatic RA, the panel strongly recommends DMARD monotherapy over double or triple DMARD therapy in patients with low disease activity and conditionally recommends DMARD monotherapy over double or triple DMARD therapy in patients with moderate or high disease activity. Methotrexate should be the preferred initial therapy for most patients with early RA with active disease.
- For patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids), the panel strongly recommends treatment with a combination of DMARDs or a TNFi or a non-TNF biologic, with or without methotrexate (MTX) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to superior efficacy.
- For patients with moderate or high disease activity despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids (defined as ≤10 mg/day of prednisone or equivalent). Low-dose glucocorticoids may also be used in patients who need a bridge until realizing the benefits of DMARD therapy. The risk/benefit ratio of glucocorticoid therapy is favorable as long as the dose is low and the duration of therapy is short.
- For patients experiencing a flare of RA, the panel conditionally recommends adding short-term glucocorticoids (<3 months of treatment) at the lowest possible dose for the shortest possible duration, to provide a favorable benefit-risk ratio for the patient.

**Recommendations for Established RA Patients**

- The panel strongly recommends using a treat-to-target strategy rather than a non-targeted approach, regardless of disease activity level. The ideal target should be low disease activity or remission, as determined by the clinician and the patient. In some cases, however, another target may be chosen because tolerance by patients or comorbidities may mitigate the usual choices.
- For DMARD-naïve patients with low disease activity, the panel strongly recommends using DMARD monotherapy over a TNFi. For DMARD-naïve patients with moderate or high disease activity, the panel conditionally recommends DMARD monotherapy over double or triple DMARD therapy and DMARD monotherapy over tofacitinib. In general, MTX should be the preferred initial therapy for most patients with established RA with active disease.
- For patients with moderate or high disease activity despite DMARD monotherapy including methotrexate, the panel strongly recommends using combination DMARDs or adding a TNFi or a non-TNF biologic or tofacitinib (all choices with or
Infliximab (Avsola™, Inflectra®, Remicade®, & Renflexis®) in no particular order of preference, rather than continuing DMARD monotherapy alone. Biologic therapy should be used in combination with MTX over biologic monotherapy, when possible, due to its superior efficacy.

For All Scenarios for Established RA Below, Treatment May Be With or Without MTX

- For moderate or high disease activity despite TNFi therapy in patients currently not on a DMARD, the panel strongly recommends that one or two DMARDs be added to TNFi therapy rather than continuing TNFi therapy alone.
- If disease activity is moderate or high despite single TNFi biologic therapy, the panel conditionally recommends using a non-TNF biologic.
- If disease activity is moderate or high despite non-TNF biologic therapy, the panel conditionally recommends using another non-TNF biologic. However, if a patient has failed multiple non-TNF biologics and they are TNFi-naïve with moderate or high disease activity, the panel conditionally recommends treatment with a TNFi.
- For patients with moderate or high disease activity despite prior treatment with at least one TNFi and at least one non-TNF-biologic (sequentially, not combined), the panel conditionally recommends first treating with another non-TNF biologic. However, when a non-TNF biologic is not an option (e.g., patient declines non-TNF biologic therapy due to inefficacy or side effects), the panel conditionally recommends treatment with tofacitinib.
- If disease activity is moderate or high despite the use of multiple (2+) TNFi therapies (in sequence, not concurrently), the panel conditionally recommends non-TNF biologic therapy and then conditionally treating with tofacitinib when a non-TNF biologic is not an option.
- If disease activity is moderate or high despite any of the above DMARD or biologic therapies, the panel conditionally recommends adding low-dose glucocorticoids.
- If patients with established RA experience an RA flare while on DMARD, TNFi, or non-TNF biologic therapy, the panel conditionally recommends adding short-term glucocorticoids (< 3 months of treatment) at the lowest possible dose and for shortest possible duration to provide the best benefit-risk ratio for the patient.

Recommendations for RA Patients with High-Risk Comorbidities

Congestive Heart Failure

- In patients with established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF), the panel conditionally recommends using combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than a TNFi.
- If patients in this population are treated with a TNFi and their CHF worsens while on the TNFi, the panel conditionally recommends switching to combination DMARD therapy, a non-TNF biologic or tofacitinib rather than a different TNFi.

Hepatitis B

- In patients with established RA with moderate or high disease activity and evidence of active hepatitis B infection (hepatitis surface antigen positive > 6 months), who are receiving or have received effective antiviral treatment, the panel strongly recommends treating them the same as patients without this condition.
- For a patient with natural immunity from prior exposure to hepatitis B (i.e., HB core antibody and HBS antibody positive and normal liver function tests), the panel recommends the same therapies as those without such findings as long as the patient’s viral load is monitored.
- For patients with chronic hepatitis B who are untreated, referral for antiviral therapy is appropriate prior to immunosuppressive therapy.

Hepatitis C

- In patients with established RA with moderate or high disease activity and evidence of chronic hepatitis C virus (HCV) infection, who are receiving or have received effective antiviral treatment, the panel conditionally recommends treating them the same as the patients without this condition.
The panel recommends that rheumatologists work with gastroenterologists and/or hepatologists who would monitor patients and reassess the appropriateness of antiviral therapy. This is important considering the recent availability of highly effective therapy for HCV, which may lead to a greater number of HCV patients being treated successfully.

If the same patient is not requiring or receiving antiviral treatment for their hepatitis C, the panel conditionally recommends using DMARD therapy rather than TNFi.

Malignancy

- **Previous Melanoma and Non-Melanoma Skin Cancer**
  - In patients with established RA and moderate or high disease activity and a history of previously treated or untreated skin cancer (melanoma or non-melanoma), the panel conditionally recommends the use of DMARD therapy over biologics or tofacitinib.

- **Previous Lymphoproliferative Disorders**
  - In patients with established RA with moderate or high disease activity and a history of a previously treated lymphoproliferative disorder, the panel strongly recommends using rituximab rather than a TNFi and conditionally recommends using combination DMARD therapy, abatacept or tocilizumab rather than TNFi.

- **Previous Solid Organ Cancer**
  - In patients with established RA with moderate or high disease activity and previously treated solid organ cancer, the panel conditionally recommends that they be treated for RA just as one would treat an RA patient without a history of solid organ cancer.

Serious Infections

- In patients with established RA with moderate or high disease activity and previous serious infection(s), the panel conditionally recommends using combination DMARD therapy or abatacept rather than TNFi.

Juvenile Idiopathic Arthritis

The 2011 American College of Rheumatology (ACR) Recommendations for the Treatment of Juvenile Idiopathic Arthritis include the tumor necrosis factor (TNF) inhibitors adalimumab, etanercept, infliximab, and do not differentiate between the agents. For JIA patients with history of arthritis of 4 or fewer joints:

- Initiation of a TNF inhibitor was recommended for patients who have received glucocorticoids joint injections and 3 months of methotrexate at the maximum tolerated typical dose and have moderate or high disease activity and features of poor prognosis (level C).
- Initiation of a TNF inhibitor was also recommended for patients who have received glucocorticoids joint injections and 6 months of methotrexate and have high disease activity without features of poor prognosis (level C).
- Initiation of a TNF inhibitor was recommended for patients specifically with the enthesitis-related arthritis category of JIA who have received glucocorticoids joint injections and an adequate trial of sulfasalazine (without prior methotrexate) and have moderate or high disease activity, irrespective of prognostic features (level C).

For JIA patients with history of arthritis of 5 or more joints:

- Initiation of a TNF inhibitor was recommended for patients who have received methotrexate or leflunomide for 3 months at the maximum tolerated typical dose and have moderate or high disease activity, irrespective of poor prognostic features (level B).
- Initiation of a TNF inhibitor was also recommended for patients who have received methotrexate or leflunomide for 6 months and have low disease activity, irrespective of poor prognostic features (level B).
- Switching from one TNF inhibitor to another was recommended as one treatment approach for patients who have received the current TNF inhibitor for 4 months and have moderate or high disease activity, irrespective of poor prognostic features (level C).
- Switching to a TNF inhibitor was recommended as one treatment approach for patients who have received abatacept for 3 months and have high disease activity and features of poor prognosis and for patients who have received abatacept for 6 months and have moderate or high disease activity, irrespective of prognostic features (level D).

Level of evidence “B” was assigned when the recommendation was supported by nonrandomized controlled studies (e.g., cohort and case–control studies) or extrapolations from randomized clinical trials.
Level of evidence “C” was assigned when the recommendation was supported by uncontrolled studies (case series),
extrapolations from nonrandomized controlled studies, or marked extrapolations from randomized clinical trials (e.g., studies of
adult arthritis patients applied to juvenile arthritis or studies of polyarthritis phenotype applied to oligoarthritis).

Noninfectious Uveitis
In 2014, a subcommittee of the Executive Committee of the American Uveitis Society conducted a systematic review of
published literature and developed a guideline for the use of anti-tumor necrosis factor α (TNF-α) biologic agents in patients
with ocular inflammatory disorders. There recommendations are as follows:

- Strong recommendation. Anti-TNF therapy with infliximab (good-quality evidence) or adalimumab (moderate-quality
evidence) should be considered early in management of patients with vision threatening ocular manifestations of Behçet’s
disease.
- Strong recommendation. Anti-TNF therapy with infliximab (good-quality evidence) or adalimumab (good-quality evidence)
should be considered as second-line immunomodulatory therapy for children with vision-threatening uveitis secondary to
JIA in whom methotrexate therapy is insufficiently effective or not tolerated. Methotrexate therapy, if tolerated, may be
combined with infliximab therapy.
- Strong recommendation. Anti-TNF therapy with infliximab or potentially adalimumab should be considered as second-line
immunomodulatory therapy in patients with vision-threatening chronic uveitis from seronegative spondyloarthropathy
(good-to moderate-quality evidence).
- Discretionary recommendation. Anti-TNF therapy with infliximab or adalimumab for other forms of ocular inflammation,
including sarcoidosis, scleritis, and panuveitis, may be considered in patients with vision-threatening, corticosteroid-
dependent disease who have failed first-line immunomodulatory therapies such as antimetabolites or calcineurin inhibitors
(moderate-quality evidence). The literature for adalimumab is less developed than for infliximab, but these agents seem to
show similar efficacy in most studies. Until more comparative data are available, no recommendation can be made as to
preferred agent, although numerous studies have suggested that adalimumab may be effective in patients who have
become intolerant to or have developed reduced clinical responsiveness to infliximab.
- Strong recommendation. Use of infliximab or adalimumab should be considered before etanercept therapy for treatment of
ocular inflammatory disease. Etanercept may have efficacy for treatment of some forms of ocular inflammatory disease
such as mucocutaneous Behçet’s disease, but it has been associated with development of uveitis in JIA patients and
development of sarcoïd-like disease in others. Patients presently taking etanercept for other indications with existing,
icompletely controlled uveitis or new ocular inflammatory disease should consider switching to infliximab or adalimumab if
possible.

Technology Assessments
A 2020 Cochrane review was published to compare the efficacy and safety of conventional systemic agents, small molecules,
and biologics for patients with moderate to severe psoriasis.24 The technical assessment also sought to provide a ranking of
these treatments according to their efficacy and safety. The assessment included 140 studies (31 new studies for the update) in
the review (51,749 randomized participants, 68% men, mainly recruited from hospitals). Nineteen treatments were assessed. At
class level, in terms of reaching PASI 90, the biologic treatments anti-IL17, anti-IL12/23, anti-IL23, and anti-TNF alpha were
significantly more effective than the small molecules and the conventional systemic agents. At drug level, in terms of reaching
PASI 90, infliximab, all of the anti-IL17 drugs (ixekizumab, secukinumab, bimekizumab, and brodalumab) and the anti-IL23
drugs (risankizumab and guselkumab, but not tildrakizumab) were significantly more effective in reaching PASI 90 than
ustekinumab and 3 anti-TNF alpha agents: adalimumab, certolizumab and etanercept. Adalimumab and ustekinumab were
significantly more effective in reaching PASI 90 than certolizumab and etanercept. There was no significant difference between
tofacitinib or apremilast and between two conventional drugs: ciclosporin and methotrexate. The network meta-analysis also
showed that infliximab, ixekizumab, risankizumab, bimekizumab, guselkumab, secukinumab and brodalumab outperformed
other drugs when compared to placebo in reaching PASI 90. The authors review showed that compared to placebo, the
biologics infliximab, ixekizumab, risankizumab, bimekizumab, guselkumab, secukinumab, and brodalumab were the best
choices for achieving PASI 90 in people with moderate-to-severe psoriasis on the basis of moderate-to high-certainty evidence
(low-certainty evidence for bimekizumab).
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 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 patients with moderately to severely active disease.

- **Psoriatic Arthritis:**
  - Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.

- **Ankylosing Spondylitis:**
  - Reducing signs and symptoms in patients with active disease.

Avsola (infliximab-axxq), Inflectra (infliximab-dyyb), and Renflexis (infliximab-abda) are biosimilar* to Remicade (infliximab). Avsola, Inflectra and Renflexis are 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 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 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 in patients with psoriatic arthritis.

● 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.

*Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product.

<table>
<thead>
<tr>
<th>Reference Product</th>
<th>Biosimilar Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remicade</td>
<td>Avsola, Inflectra, Ixifi, Renflexis</td>
</tr>
</tbody>
</table>

The FDA issued an alert dated September 7, 2011, to inform healthcare professionals that the Boxed Warning for the entire class of Tumor Necrosis Factor-alpha (TNFα) blockers has been updated to include the risk of infection from two bacterial pathogens, *Legionella* and *Listeria*. In addition, the Boxed Warning and Warnings and Precautions sections of the labels for all of the TNFα blockers have been revised so that they contain consistent information about the risk for serious infections and the associated disease-causing pathogens.¹¹

The FDA issued an update on November 3, 2011 regarding their ongoing safety review of Tumor Necrosis Factor (TNF) blockers and malignancy in children, adolescents, and young adults (30 years of age or younger). This issue was previously communicated in June 2008, August 2009, and April 2011. The FDA is requiring the manufacturers of TNF blockers to perform enhanced safety surveillance for these products. The manufacturers will also provide FDA with annual summaries and assessments of malignancies and TNF blocker utilization data. Healthcare professionals should remain vigilant for cases of malignancy in patients treated with TNF blockers.¹⁰

---

**Centers for Medicare and Medicaid Services (CMS)**

Medicare does not have a National Coverage Determination (NCD) for Infliximab (Avsola™, Inflectra®, Remicade®, and Renflexis®). Local Coverage Determinations (LCDs)/Local Coverage Articles (LCAs) exist; refer to the LCDs/LCAs for Infliximab and Drugs and Biologicals, Coverage of, for Label and Off-Label Uses.

In general, Medicare may cover outpatient (Part B) drugs that are “incident to” a physician’s service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals. (Accessed July 6, 2021)

* *Preferred therapy criteria for Medicare Advantage members, refer to Medicare-Part-B-Step-Therapy-Programs.

**References**


Policy History/Revision Information

<table>
<thead>
<tr>
<th>Date</th>
<th>Summary of Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/01/2022</td>
<td>Coverage Rationale</td>
</tr>
<tr>
<td></td>
<td>Preferred Product: Medical Necessity Plans</td>
</tr>
<tr>
<td></td>
<td>Revised medical necessity criteria for treatment with Remicade, Renflexis, or other non-preferred infliximab biosimilar; added criterion to allow coverage when the patient is breastfeeding</td>
</tr>
<tr>
<td></td>
<td>Supporting Information</td>
</tr>
<tr>
<td></td>
<td>Archived previous policy version 2022D0004AJ</td>
</tr>
</tbody>
</table>

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare 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. UnitedHealthcare 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.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual™ criteria, to assist us in administering health benefits. UnitedHealthcare 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.