Pharmacy Prior Authorization
Clinical Guideline – Cytokines and Cell Adhesion Molecule (CAM) Antagonists

Actemra® (tocilizumab)
Cimzia® (certolizumab)
Cosentyx® (secukinumab)
Enbrel® (entanercept)
Entyvio® (vedolizumab)
Humira® (adalimumab)
Ilaris® (canakinumab)
Kineret® (anakinra)
Orencia® (abatacept)
Remicade® (infliximab)
Simponi® (golimumab)
Simponi Aria® (golimumab)
Stelara® (ustekinumab)
Taltz® (ixekizumab)
Tysabri® (natalizumab)
Xeljanz® (tofacitinib)
Xeljanz XR® (tofacitinib)

Preferred Agents: ENBREL and HUMIRA are the preferred agents. Requests for non-preferred anti-TNFs (Cimzia, Remicade, and Simponi) require trial and failure of BOTH Enbrel and Humira (where both are indicated) in addition to all other clinical criteria. Requests for other non-preferred cytokines and CAM antagonists require trial and failure of either Enbrel or Humira (where indicated) in addition to all other clinical criteria. NOTE: The authorization criteria for Tysabri in multiple sclerosis is included in the MS agents PA guideline.

General Authorization Guidelines for All Medications and Indications:

- Patient is NOT on another cytokine or CAM antagonist
- Prescribed by an appropriate specialist based on indication
- Patient has been evaluated for and given the appropriate vaccinations as recommended per the CDC for his/her risk factors
- Patient has been screened for tuberculosis (TB). If screening was positive for latent TB, patient has received treatment for latent TB.
- The prescribed dose is FDA-approved for the indication. Doses above the FDA-approved labeling will not be authorized. Quantity limits exist.
- For anti-TNFs only: Patient does NOT have NYHA class III or IV CHF
- For anti-TNFs, Stelara, Xeljanz, Kineret, Actemra, Ilaris, and Orencia: Patient has been screened for hepatitis B. If patient has active or chronic hepatitis B, the patient is receiving appropriate antiviral treatment
- For Entyvio and Tysabri: Will be used as monotherapy and NOT in combination with antineoplastic, immunosuppressive, or immunomodulating agents (e.g., azathioprine, 6-mercaptopurine cyclosporine, methotrexate, TNF-inhibitors)
- For Actemra:
    - Patient has an absolute neutrophil count (ANC) $\geq$2000 per mm^3.
    - Patient has a platelet count $\geq$100,000 per mm^3.
    - Patient does NOT have elevated ALT or AST >1.5× ULN.

Additional Criteria Based on Indication:

- **Rheumatoid Arthritis (RA): (Enbrel, Humira, Cimzia, Remicade, Simponi, Simponi Aria, Kineret, Orencia, Xeljanz, Actemra)**
    - Patient is at least 18 years old
    - Patient has moderate or high disease activity despite an adequate 3-month trial of 2 different non-biologic DMARD regimens (1 of which must include methotrexate (MTX) unless contraindicated)
        - Monotherapy: MTX, sulfasalazine (SSZ), or leflunomide (LEF)
        - Combination: MTX+SSZ+hydroxychloroquine (HCQ), MTX+HCQ, MTX+LEF, MTX+SSZ, SSZ+HCQ
- **Systemic Juvenile Idiopathic Arthritis: (Enbrel, Humira, Orencia IV)**
    - Age Restriction (Enbrel and Humira): Patient is at least 2 years old

  - Age Restriction (Orencia): Patient is at least 6 years old
  - Patient does NOT have currently ACTIVE systemic features (i.e., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis) but has continued synovitis in ≥1 joint despite treatment for 3 months with MTX or leflunomide
- **Systemic Juvenile Idiopathic Arthritis: (Kineret and Actemra IV)**
  - Patient is at least 2 years old
  - Patient does NOT have currently ACTIVE systemic features (i.e., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis) but has continued synovitis in ≥1 joint despite treatment for 3 months with MTX or leflunomide; **OR**
  - Patient currently has ACTIVE systemic features (i.e., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis) AND synovitis in at least 1 joint
  - NOTE: Patient does not require trial of Enbrel or Humira
- **Systemic Juvenile Idiopathic Arthritis: (Ilaris)**
  - Patient is at least 2 years old and weighs at least 7.5kg
  - Patient currently has ACTIVE systemic features (i.e., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis)
  - Patient has continued synovitis in >1 joint despite treatment for at least 1 month with Kineret or Actemra AND methotrexate or leflunomide (Note: both Kineret and Actemra are also non-formulary and require PA)
  - NOTE: Patient does not require trial of Enbrel or Humira
- **Polyarticular Juvenile Idiopathic Arthritis: (Enbrel, Humira, Orencia IV, Actemra IV)**
  - Age Restriction (Enbrel, Humira, and Actemra): Patient is at least 2 years old
  - Age Restriction (Orencia): Patient is at least 6 years old
  - Patient has severe disease OR moderate to severe disease despite an adequate 3-month trial of MTX
- **Oligoarticular Juvenile Idiopathic Arthritis: (Enbrel, Humira)**
  - NOTE: anti-TNF's are not the standard of therapy for most patients as this is usually a self-limiting condition that rarely becomes chronic
  - Patient is at least 2 years old
  - Patient has extended oligoarticular JIA (defined as disease duration > 6 months)
  - Patient had inadequate response or intolerable side effects with 2 NSAIDs or has contraindications to NSAIDs.
  - Patient had inadequate response or intolerable side effects with an adequate 3-month trial of MTX or has contraindications to MTX.
- **Cryopyrin-Associated Periodic Syndromes (CAPS): (Kineret)**
  - Diagnosis has been confirmed by positive genetic test for NALP3, CIAS1, or NLRP3 mutation
  - NOTE: Patient does not require trial of Enbrel or Humira
- **Cryopyrin-Associated Periodic Syndromes (CAPS): (Ilaris)**
  - Patient is at least 4 years old and weighs at least 15kg
  - Diagnosis has been confirmed by positive genetic test for NALP3, CIAS1, or NLRP3 mutation
  - Patient has failed a 3-month minimum trial of Kineret (Note: Kineret is also non-formulary and requires PA)
  - NOTE: Patient does not require trial of Enbrel or Humira

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- **Ankylosing Spondylitis (AS): (Enbrel, Humira, Cimzia, Remicade, Simponi, Cosentyx)**
  - Patient is at least 18 years old
  - Patient has unacceptable disease activity despite a 3-month trial of TWO different NSAIDs at an adequate dose OR has a contraindication to NSAID use
  - Patient will be continued on an NSAID when cytokine or CAM antagonist is initiated (unless contraindicated)
- **Psoriatic Arthritis (PsA): (Enbrel, Humira, Cimzia, Remicade, Simponi, Cosentyx, Stelara)**
  - Patient is at least 18 years old
  - Patient is currently on an NSAID and will be continued OR has a contraindication to NSAID use
  - Patient meets ONE of the following:
    - Has active PsA despite a 3-month trial of adequate dose MTX (or leflunomide or sulfasalazine if MTX is contraindicated)
    - Patient has predominantly axial disease or active enthesitis/dactylitis AND has unacceptable disease activity despite a 3-month trial of TWO different NSAIDs at an adequate dose (unless contraindicated)
- **Plaque Psoriasis: (Enbrel, Humira, Remicade, Cosentyx, Taltz, Stelara)**
  - Patient is at least 18 years old (Humira, Remicade, Cosentyx, Taltz, Stelara)
  - Patient is at least 6 years old (Enbrel)
  - Symptoms are not controlled with topical therapy
  - Disease has a significant impact on physical, psychological or social wellbeing
  - Patient has failed a 3-month compliant trial with MTX or cyclosporine or has a true contraindication to both
  - Psoriasis is severe and extensive (for example, more than 10% of body surface area affected or a PASI score of more than 10)
  - Phototherapy has been ineffective, cannot be used or has resulted in rapid relapse (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months)
- **Ulcerative Colitis (UC): (Humira, Remicade, Simponi, Entyvio)**
  - Age restriction (Humira, Simponi, and Entyvio): At least 18 years old
  - Age restriction (Remicade): At least 6 years old
  - STEROID-DEPENDENT UC :
    - Patient had a relapse within three months of stopping glucocorticoids OR is unable to taper steroids to an acceptable dose after 3 months without having symptom recurrence
    - Patient had inadequate response or intolerable side effects with a 3-month trial of 6-mercaptopurine (6-MP) or azathioprine (AZA) or has contraindications to both
  - STEROID-REFRACTORY UC:
    - Inadequate response or intolerable side effects to IV glucocorticoids after 7-10 days OR oral prednisone ≥40mg/day after 30 days
    - Patient meets ONE of the following:
      - Patient had a previous failure on 6-MP and AZA or a contraindication to both medications and is therefore not a candidate for treatment with these agents for current episode

  - Patient had an inadequate response or intolerable side effects to cyclosporine or there is a contraindication (NOTE: cyclosporine is used as a bridge therapy for patients who will be started on the slower acting 6-MP or AZA)
  - Patient has had surgical intervention
- **Additional Criteria for Crohn's: (Humira, Remicade, Cimzia, Stelara, Entyvio, Tysabri)**
  - Age restriction (Cimzia, Stelara, Entyvio, and Tysabri): At least 18 years old
  - Age restriction (Remicade and Humira): At least 6 years old
  - STEROID-DEPENDENT CROHN'S :
    - Patient had a relapse within three months of stopping glucocorticoids OR is unable to taper steroids to an acceptable dose after 3 months without having symptom recurrence
    - Patient had inadequate response or intolerable side effects with a 3-month trial of 6-mercaptopurine (6-MP) or azathioprine (AZA) or injectable MTX or has contraindications to all agents
  - STEROID-REFRACTORY CROHN'S:
    - Inadequate response or intolerable side effects to IV glucocorticoids after 7-10 days OR oral prednisone ≥40mg/day after 30 days (NOTE: it is recommended to switch to IV glucocorticoids for patients who are not responding to oral glucocorticoids)
- **Additional Criteria for Hidradenitis Suppurative (acne inversa): (Humira)**
  - Patient is at least 18 years old
  - Patient has ≥3 abscesses or inflammatory nodules
  - Patient has moderate to severe disease (Hurley stage II-III)
  - Patient has had inadequate response or intolerable side effects with an oral antibiotic such as tetracycline, doxycycline, or minocycline OR topical antibiotics (if patient has a contraindication to oral tetracyclines)
- **Additional Criteria for Uveitis: (Humira)**
  - Patient is at least 18 years old
  - Patient has intermediate, posterior, or panuveitis that is not caused by an infection
  - Patient is currently taking an oral corticosteroid or has a contraindication to corticosteroids
  - Patient has had an inadequate response or intolerable side effects with at least 2 different steroid-sparing immunosuppressive medications such as methotrexate, azathioprine, mycophenolate, cyclosporine, or tacrolimus, or has contraindications to these agents

Initial Approval:

4 months

Renewal:

Indefinite

- UC and Crohn's: Patient should be in remission without need for daily prednisone >5 mg per day
- RA, JIA, AS, PsA, uveitis: At least 20% symptom improvement
- Psoriasis: At least 20% improvement. Enbrel dose should be reduced to 50mcg per week
- Hidradenitis: At least 25% reduction in total abscess and inflammatory nodule count AND no increase in abscesses or draining fistulas

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- Labs required for Actemra:
  - ANC ≥500 per mm^3
  - Platelets ≥50,000 per mm^3
  - ALT and AST are ≤5× ULN

Quantity Limits:

- Humira:
  - For RA, AS, PsA, and JIA: 2 syringes/pens per 28 days
  - For Crohns, UC, and Hidradenitis:
    - 6 syringes/pens in the initial 28 days
    - 2 syringes/pens per 28 days after induction period
  - For Psoriasis and Uveitis:
    - 4 syringes/pens in the initial 28 days
    - 2 syringes/pens per 28 days after induction period
- Enbrel:
  - For RA, AS, PsA, and JIA: 4, 50mg syringes OR 8, 25mg syringes per 28 days
  - For Psoriasis:
    - 8, 50mg syringes per 28 days for the initial 3 months
    - 4, 50mg syringes per 28 days after induction period
- Actemra SQ:
  - For RA:
    - Weight <100kg: 2 syringes per 28 days. Max dose is 4 syringes per 28 days
    - Weight ≥100kg: 4 syringes per 28 days
- Actemra IV:
  - For RA: 4 to 8mg/kg every 28 days
  - For PJIA:
    - Weight <30kg: 10mg/kg every 28 days
    - Weight ≥30kg: 8mg/kg every 28 days
  - For SJIA:
    - Weight <30kg: 12mg/kg every 14 days
    - Weight ≥30kg: 8mg/kg every 14 days
- Cimzia:
  - 6 syringes/vials allowed in the initial 54 days
  - 2 syringes/vials per 28 days after induction period
- Cosentyx
  - For AS and PsA:
    - 4 syringes/pens in the initial 28 days
    - 1 syringe/pen per 28 days after induction period
  - For Psoriasis:
    - 8 syringes/pens in the initial 28 days
    - 2 syringes/pens per 28 days after induction period
- Entyvio
  - For Crohns and UC: 1 vial per 28 days for the initial 2 months; then 1 vial per 56 days

- Ilaris:
  - For CAPS (>40 kg): 150mg every 8 weeks, 1 vial per 56 days
  - For CAPS (≤40 kg): 2mg/kg every 8 weeks, 1 vial per 56 days. Dose may be increased to 3mg/kg given every 8 weeks
  - For SJIA: 4mg/kg (max 300mg) every 4 weeks
    - QLL for doses <180mg: 1 vial per 28 days
    - QLL for doses >180mg: 2 vials per 28 days
- Kineret:
  - For RA, JIA, and CAPS: 1 syringe per day
- Orencia IV:
  - For RA:
    - Weight <60kg: 2 vials per 28 days
    - Weight 60-100kg: 3 vials per 28 days
    - Weight >100kg: 4 vials per 28 days
  - For JIA:
    - Weight <75kg: 10mg/kg every 28 days
    - Weight >75kg: Follow adult RA dosing above
- Orencia SQ:
  - For RA: 4 syringes per 28 days
- Remicade:
  - For RA: 3mg/kg at week 0, 2 and 6, then every 8 weeks thereafter. Max dose is 10mg/kg every 8 weeks or 3mg/kg every 4 weeks.
  - For Crohns: 5mg/kg at week 0, 2 and 6, then every 8 weeks thereafter. Max dose is 10mg/kg every 8 weeks
  - For UC, PsA and Psoriasis: 5mg/kg at week 0, 2 and 6, then every 8 weeks thereafter.
  - For AS: 5mg/kg at week 0, 2 and 6, then every 6 weeks thereafter.
- Simponi:
  - For RA, AS, and PsA: 1, 50mg syringe per 28 days
  - For UC:
    - 3, 100mg syringes allowed in the initial 54 days
    - 1, 100mg syringe per 28 days after induction period
- Simponi Aria:
  - For RA: 2mg/kg at week 0 and 4, then every 8 weeks thereafter
- Stelara:
  - For Psoriasis:
    - Weight ≤100kg: 1, 45mg syringe per 28 days for initial 2 months; then 1, 45mg syringe per 84 days
    - Weight >100kg: 1, 90mg syringe per 28 days for initial 2 months; then 1, 90mg syringe per 84 days
  - For PsA:
    - 1, 45mg syringe per 28 days for initial 2 months; then 1, 45mg syringe per 84 days
  - For Crohns:
    - 1, 90mg syringe per 56 days

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- Taltz
  - For Psoriasis:
    - 3 syringes in the first 28 days
    - 2 syringes per 28 days for months 2 and 3
    - 1 syringe per 28 days after initial induction
- Tysabri:
  - For Crohns: 1 vial per 28 days
- Xeljanz:
  - For RA: 2 tablets per day
- Xeljanz XR:
  - For RA: 1 tablet per day

References:

1. Enbrel (etanercept) [package insert]. Thousand Oaks, CA; Immunex Corporation; Revised March 2015.
2. Humira (adalimumab) [package insert]. North Chicago, IL; AbbVie Inc; Revised August 2016.
3. Cimzia (certolizumab) [package insert]. Smyrna, GA; UCB Inc; Revised May 2016.
4. Remicade (infliximab) [package insert]. Horsham, PA; Janssen Biotech Inc; Revised September 2015.
5. Simponi (golimumab) [package insert]. Horsham, PA; Janssen Biotech Inc; Revised June 2015.
6. Orencia (abatacept) [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; Revised June 2015.
7. Xeljanz (tafacitinib citrate) [package insert]. NJ, NJ; Pfizer Labs; Revised March 2016.
8. Stelara (ustekinumab) [package insert]. Horsham, PA: Janssen Biotech, Inc. Revised September 2016.
9. Kineret (anakinra) [package insert]. Stockholm, Sweden; Swedish Orphan Biovitrum AB; Revised July 2015.
10. Actemra (tocilizumab) [package insert]. South San Francisco, CA; Genetec, Inc; Revised September 2016.
11. Ilaris (canakinumab) [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation; Revised July 2016.
12. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Care Res*. 2016;68(1):1-25.
13. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis Care Res*. 2013;65(10):1551-1563.
14. Weiss PF. Polyarticular juvenile idiopathic arthritis: Clinical manifestations and diagnosis. Waltham, MA: UptoDate; Last modified September 29, 2015. http://www.uptodate.com/contents/polyarticular-juvenile-idiopathic-arthritis-treatment?source=search_result&search=juvenile+arthritis&selectedTitle=8%7E150. Accessed October 5, 2015.
15. Kimura Y. Systemic juvenile idiopathic arthritis: Treatment. Waltham, MA: UptoDate; Last modified August 15, 2016. https://www.uptodate.com/contents/systemic-juvenile-idiopathic-arthritis-treatment?source=search_result&search=juvenile+idiopathic+arthritis&selectedTitle=6%7E150. Accessed September 22, 2016.
16. Weiss PF. Oligoarticular juvenile idiopathic arthritis. Waltham, MA: UptoDate; Last modified December 9, 2015. https://www.uptodate.com/contents/oligoarticular-juvenile-idiopathic-arthritis?source=search_result&search=juvenile+idiopathic+arthritis&selectedTitle=4%7E150. Accessed September 22, 2016.
17. National Institute for Health and Clinical Excellence (NICE). Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2016 Dec. 58 p. (NICE technology appraisal guideline; no. 373).

18. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Care Res*. 2016;68(2):282-298.
19. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis.* 2015;0:1-12.
20. National Institute for Health and Clinical Excellence (NICE). Psoriasis: the assessment and management of psoriasis. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012 Oct. 61 p. (NICE clinical guideline; no. 153).
21. Feldman SR. Treatment of psoriasis. Waltham, MA: UptoDate; Last modified July 13, 2015. http://www.uptodate.com/contents/treatment-of-psoriasis?source=search_result&search=psoriasis&selectedTitle=1%7E150#H42. Accessed September 25, 2015.
22. National Institute for Health and Clinical Excellence (NICE). Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (including a review of TA140 and TA262). London (UK): National Institute for Health and Clinical Excellence (NICE); 2015 Feb. 70 p. (NICE technology appraisal guideline; no. 329).
23. Cohen RD., Stein AC. Approach to adults with steroid-refractory and steroid-dependent ulcerative colitis. Waltham, MA: UpToDate; Last modified June 2016. https://www.uptodate.com/contents/approach-to-adults-with-steroid-refractory-and-steroid-dependent-ulcerative-colitis?source=search_result&search=ulcerative%20colitis&selectedTitle=4~150#H14. Accessed October 5, 2016.
24. Peppercorn MA., Farrell RJ. Management of severe ulcerative colitis in adults. Waltham, MA: UpToDate; Last modified September 2016. https://www.uptodate.com/contents/management-of-severe-ulcerative-colitis-in-adults?source=search_result&search=ulcerative%20colitis&selectedTitle=3~150#H1133536041. Accessed October 5, 2016.
25. Bousvaros A., Russell GH., Setty M. Management of severe or refractory ulcerative colitis in children and adolescents. Waltham, MA: UpToDate; Last modified October 2015. https://www.uptodate.com/contents/management-of-severe-or-refractory-ulcerative-colitis-in-children-and-adolescents?source=search_result&search=ulcerative%20colitis&selectedTitle=8~150. Accessed October 5, 2016.
26. The Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults. *Am J Gastroenterol.* 2010;105:501-523.
27. Farrell RJ, Peppercorn MA. Overview of the medical management of severe or refractory Crohn disease in adults. Waltham, MA: UpToDate; Last modified January 14, 2016. https://www.uptodate.com/contents/overview-of-the-medical-management-of-severe-or-refractory-crohn-disease-in-adults?source=search_result&search=crohn&selectedTitle=3~150. Accessed October 5, 2016.
28. Bousvaros A. Overview of the management of Crohn disease in children and adolescents. Waltham, MA: UpToDate; Last modified August 25, 2016. https://www.uptodate.com/contents/overview-of-the-management-of-crohn-disease-in-children-and-adolescents?source=search_result&search=crohn&selectedTitle=4~150. Accessed October 5, 2016.
29. American Gastroenterological Association Institute Clinical Practice and Quality Management Committee. American Gastroenterological Association Institute Guideline on the use of thiopurines, methotrexate, and anti–TNF-a biologic drugs for the induction and maintenance of remission in inflammatory crohn's disease. *Gastroenterol.* 2013;145:1459–1463.
30. Margesson LJ, Danby FW. Treatment of hidradenitis suppurativa (acne inversa). Waltham, MA: UptoDate; Last modified September 25, 2015. http://www.uptodate.com/contents/treatment-of-hidradenitis-suppurativa-acne-inversa?source=search_result&search=hidradenitis+suppurativa&selectedTitle=1%7E46#H9540636. Accessed October 5, 2015.
31. National Institute for Health and Clinical Excellence (NICE). Adalimumab for treating moderate to severe hidradenitis suppurative. London (UK): National Institute for Health and Clinical Excellence (NICE); 2016 June. 43 p. (NICE technology appraisal guideline; no. 392).

32. Rosenbaum JT. Uveitis: Treatment. Waltham, MA: UptoDate; Last updated August 3, 2016. https://www.uptodate.com/contents/uveitis-treatment?source=search_result&search=uveitis&selectedTitle=2%7E150. Accessed September 21, 2016.