Aetna Better Health®

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

Actemra (tocilizumab)
Arcalyst (rilonacept)
Cimzia (certolizumab)
Cosentyx (secukinumab)
Enbrel (etanercept)
Entyvio (vedolizumab)
Humira (adalimumab)
Ilaris (canakinumab)
Ilumya (tildrakizumab)
Inflectra (infliximab-dyyb)
Kevzara (sarilumab)
Kineret (anakinra)
Olumiant (baricitinib)
Orencia (abatacept)
Remicade (infliximab)
Renflexis (infliximab-adba)
Siliq (brodalumab)
Simponi (golimumab)
Simponi Aria (golimumab)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tremfya (guselkumab)
Tysabri (natalizumab)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib)

Preferred Agents: ENBREL HUMIRA, and KEVZARA are the preferred agents.

Requests for Non-Preferred Anti-Tumor Necrosis Factors (TNFs) (Cimzia, Remicade, Inflectra, Renflexis and Simponi) require trial and failure of all preferred agents (Enbrel, Humira and Kevzara), where indicated, in addition to all other clinical criteria.

Requests for other Non-Preferred Cytokines and Cell Adhesion Molecule (CAM) Antagonists require trial and failure of either Enbrel, Humira or Kevzara (where indicated), in addition to all other clinical criteria.

NOTE: The authorization criteria for Tysabri in multiple sclerosis are included in the Multiple Sclerosis agents Prior Authorization guideline.

General Authorization Guidelines for All Medications and Indications:

- Member is not on another Cytokine or Cell Adhesion Molecule (CAM) Antagonist
- Prescribed by an appropriate specialist based on indication
- Member has been evaluated for, and given appropriate vaccinations, as recommended per Center for Disease Control for member risk factors
- Member has been screened for tuberculosis. If screening was positive for latent tuberculosis, member has received treatment for latent tuberculosis
- The prescribed dose is Food and Drug Administration (FDA) approved for the indication. Doses above the Food and Drug Administration (FDA) approved labeling will not be authorized. Quantity limits exist
- For Anti-Tumor Necrosis Factors only: Member does not have New York Heart Association (NYHA) class III or IV Congestive Heart Failure
- For Anti-Tumor Necrosis Factors, Stelara, Xeljanz, Xeljanz XR, Kineret, Actemra, Ilaris, and Orencia: Member has been screened for Hepatitis B. If member has active or chronic Hepatitis B, member is receiving appropriate antiviral treatment
- For Entyvio and Tysabri: Will be used as monotherapy and not in combination with antineoplastic, immunosuppressive, or immunomodulating agents (for example, azathioprine, 6-mercaptopurine cyclosporine, methotrexate, tumor necrosis factors (TNF) inhibitors)

Additional Criteria Based on Indication:

Rheumatoid Arthritis: (Enbrel, Humira, Actemra, Cimzia, Inflectra, Kevzara, Kineret, Olumiant, Orencia, Remicade, Renflexis, Simponi, Simponi Aria, Xeljanz, Xeljanz XR)

- Member is 18 years of age or older
- Diagnosis of active moderate to severe Rheumatoid Arthritis(for example, swollen, tender joints with limited range of motion)
- Documented inadequate response to a three month trial of 2 different non-biologic Disease-Modifying Anti-Rheumatic Drug (DMARD) regimens (one of which must include methotrexate. If there is an intolerance or contraindication to methotrexate, member can use sulfasalazine, or leflunomide
  - Monotherapy: Methotrexate, sulfasalazine, or leflunomide
  - Combination: Methotrexate + sulfasalazine +hydroxychloroquine , or methotrexate + hydroxychloroquine, or methotrexate + leflunomide, or methotrexate + sulfasalazine, or sulfasalazine + hydroxychloroquine

- **Systemic Juvenile Idiopathic Arthritis: [Enbrel, Humira, Orencia (subcutaneous/intravenous)]**
  - Member is 2 years of age or older (Enbrel, Humira, and Orencia (subcutaneous)
  - Member is 6 years -of age or older (Orencia intravenous)
  - Documentation of the following:
    - Member does not have active systemic features (for example, fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis)
    - Synovitis is in one or more joints despite a three months treatment with methotrexate, or leflunomide
- **Systemic Juvenile Idiopathic Arthritis: [Kineret, Actemra)]**
  - Member is 2 years of age or older
  - Documentation of one of the following:
    - Member does not have active systemic features (for example, fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis), and synovitis is in one or more joints despite a three months treatment with methotrexate, or leflunomide
    - Member has active systemic features (for example, fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis), and synovitis is in at least one joint
  - Member does not require trial of Enbrel or Humira
- **Systemic Juvenile Idiopathic Arthritis: (Ilaris)**
  - Member is 2 years of age or older and weighs at least 7.5 kilograms
  - Documentation of the following:
    - Member has active systemic features (for example, fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis)
    - Synovitis is in one or more joints despite a one month treatment with Kineret or Actemra, and methotrexate or leflunomide (Kineret and Actemra are Non-Formulary and will require Prior Authorization)
  - Member does not require trial of Enbrel or Humira
- **Polyarticular Juvenile Idiopathic Arthritis: [Enbrel, Humira, Orencia (intravenous/subcutaneous), Actemra]**
  - Member is 2 years of age or older (Enbrel, Humira, Orencia (subcutaneous), and Actemra)

  - Member is 6 years of age or older (Orencia (intravenous))
  - Documented inadequate response to a three months trial of methotrexate
  - If member has an intolerance, or contraindication to methotrexate, a documented trial of sulfasalazine, or leflunomide for 3 months is required
- **Oligoarticular Juvenile Idiopathic Arthritis: (Enbrel, Humira)**
  NOTE: Anti- Tumor Necrosis Factors are not standard therapy for most members, as this is usually a self-limiting condition that rarely becomes chronic
  - Member is 2 years of age or older
  - Member has extended Oligoarticular Juvenile Idiopathic Arthritis, defined as disease duration greater than 6 months
  - Documented inadequate response or intolerable side effect to two Non-Steroidal Anti-Inflammatory Drugs, or member has a contraindication to Non-steroidal Anti-Inflammatory Drugs
  - Documented inadequate response or intolerable side effect to a three month trial of methotrexate, or member has a contraindication to methotrexate
- **Cryopyrin-Associated Periodic Syndromes: (Kineret)**
  - Diagnosis of Cryopyrin-Associated Periodic Syndromes, including neonatal-onset multisystem inflammatory disease, Familial Cold Auto Inflammatory Syndrome, or Muckle-Wells Syndrome
  - NOTE: Member does not require trial of Enbrel or Humira
- **Cryopyrin-Associated Periodic Syndromes: (Arcalyst, Ilaris)**
  - Member is 4 years of age or older and weighs at least 15 kilograms (Ilaris)
  - Member is 12 years of age or older (Arcalyst)
  - Diagnosis of Cryopyrin-Associated Periodic Syndromes with one of the following subtypes
    - Familial Cold Auto Inflammatory Syndrome
    - Muckle-Wells syndrome
  - Member had a three months trial of Kineret (Kineret is Non-Formulary and will require a Prior Authorization)
- Member does not require trial of Enbrel or Humira**Familial Mediterranean Fever: (Ilaris)**
  - Member is 2 years of age or older
  - Documented inadequate response, intolerance, or contraindication to colchicine at maximum indicated dose
- **Giant Cell Arteritis: (Actemra subcutaneous)**
  - Member is 18 years of age or older
  - Documented inadequate response, intolerance, or contraindication with glucocorticoids (for example prednisone, methylprednisolone).
  - If member has an intolerance, or contraindication to glucocorticoids, a trial of methotrexate or cyclophosphamide is required
  - Actemra will be used in combination with a tapering course of glucocorticoids
- **Ankylosing Spondylitis: (Enbrel, Humira, Cimzia, Cosentyx, Inflectra, Remicade, Renflexis, Simponi, Simponi Aria)**
  - Member is 18 years of age or older

  - Documented inadequate response to a one month trial of two Non-Steroidal Anti-Inflammatory Drugs, or member has a contraindication or intolerance to oral Non-Steroidal Anti-Inflammatory Drugs
- **Psoriatic Arthritis: (Enbrel, Humira, Cimzia, Cosentyx, Inflectra, Orencia, Remicade, Renflexis, Simponi, Simponi Aria, Stelara, Taltz, Xeljanz, Xeljanz XR)**
  - Member is 18 years of age or older
  - Documentation of one of the following:
    - Member has active Psoriatic Arthritis, and an inadequate response to a three months trial of methotrexate, or if member has intolerance, or contraindication to methotrexate, a trial of sulfasalazine , or leflunomide for 3 months is required
    - Member has predominantly axial disease or active enthesitis/dactylitis, and had an inadequate response to a one month trial of two Non-Steroidal Anti-Inflammatory Drugs, or member has a contraindication or intolerance to oral Non-Steroidal Anti-Inflammatory Drugs

  Note:
  - Member should continue use of Non-Steroidal Anti-Inflammatory Drugs as needed for bridging or adjunctive therapy when starting a Disease-Modifying Anti-Rheumatic Drug
  - Cosentyx and Stelara should be considered if member has contraindication to Tumor Necrosis Factor Inhibitors (for example, Heart failure, Multiple Sclerosis), where Tumor Necrosis Factor Inhibitor is indicated
- **Plaque Psoriasis: (Enbrel, Humira, Cimzia, Cosentyx, Ilumya, Inflectra, Remicade, Renflexis, Siliq, Tremfya, Stelara, Taltz)**
  - Member is 18 years of age or older (Humira, Cosentyx, Ilumya, Inflectra, Remicade, Renflexis, Siliq, Taltz, Tremfya)
  - Member is 4 years of age or older (Enbrel)
  - Member is 12 years of age or older (Stelara)
  - Documented inadequate response, intolerance, or contraindication, to at least one oral systemic therapy such as methotrexate, or cyclosporine for 3 months or more
  - Member has one of the following:
    - More than 10% of Body Surface Area is affected
    - Less than 10% Body Surface Area is affected, but involves sensitive areas (for example, hands, feet, face or genitals) that interfere with daily activities
    - Psoriasis Area and Severity Index score more than 10
  - Phototherapy (PUVA (psoralen ultra violet type A), UVB (ultraviolet type B)) has been ineffective
  - For Siliq: Mental health evaluation has been completed by prescriber or psychiatrist, if member has history of prior suicide attempt, bipolar disorder or depressive disorder
- **Ulcerative Colitis: (Humira, Entyvio, Inflectra, Remicade, Renflexis, Simponi, Xeljanz)**
  - Member is 18 years of age or older (Humira, Entyvio, Inflectra, Simponi, Renflexis, Xeljanz)
  - Member is 6 years of age or older (Remicade)
  - <u>STEROID-DEPENDENT Ulcerative Colitis:</u>
    - Documented relapse within three months of stopping glucocorticoids, or is unable to taper steroids to an acceptable dose after 3 months, without having symptom recurrence
    - Documented inadequate response, or intolerable side effects, with a 3-month trial of mercaptopurine, or azathioprine, or has contraindication to both

- STEROID-REFRACTORY Ulcerative Colitis
  - Documented inadequate response, or intolerable side effect to intravenous glucocorticoids after 7-10 days, or oral prednisone greater than or equal to 40mg per day after 30 days
  - Member meets one of the following:
    - Documented failure of mercaptopurine, and azathioprine, or there is a contraindication to both medications, and member is not a candidate for treatment with these agents for current episode
    - Documented inadequate response, or intolerable side effect to cyclosporine, or member has contraindication to cyclosporine (NOTE: cyclosporine is used as a bridge therapy for members who will be started on slower acting mercaptopurine, or azathioprine)
    - Member had surgical intervention

- **Additional Criteria for Crohn's Disease: (Humira, Cimzia, Entyvio, Inflectra, Remicade, Renflexis, Stelara, Tysabri)**
  - Member is 18 years of age or older (Cimzia, Entyvio, Stelara, Tysabri)
  - Member is 6 years of age or older (Humira, Inflectra, Remicade, Renflexis)
  - STEROID-DEPENDENT CROHN'S :
    - Documented relapse within three months of stopping glucocorticoids, or is unable to taper steroids to an acceptable dose after 3 months without having symptom recurrence
    - Documented inadequate response, or intolerable side effect, with a 3-month trial of mercaptopurine, or azathioprine, or injectable methotrexate, or member has a contraindication to all agents
  - STEROID-REFRACTORY CROHN'S:
    - Documented inadequate response, or intolerable side effects, to intravenous glucocorticoids after 7-10 days, or oral prednisone greater than or equal to 40mg per day after 30 days (NOTE: It is recommended to switch to intravenous glucocorticoids for members that are not responding to oral glucocorticoids)
- **Additional Criteria for Hidradenitis Suppurativa (Acne Inversa): (Humira)**
  - Member is 12 years of age or older
  - Member has moderate to severe disease (Hurley stage II-III)
  - Documentation of trial and failure of a 90 day treatment with oral antibiotics (for example, doxycycline, minocycline, or clindamycin with rifampin)
- **Additional Criteria for Uveitis: (Humira)**
  - Member is 2 years of age or older
  - Member has intermediate, posterior, or pan uveitis that is not caused by an infection
  - Documented inadequate response, or intolerable side effect, with any of the following: Corticosteroids, methotrexate, azathioprine, mycophenolate, cyclosporine, tacrolimus, or medications are not appropriate
- **Additional Criteria for Cytokine Release Syndrome: (Actemra intravenous only)**
  - Member is 2 years of age or older
  - Member has Grade 4, severe or life threatening Cytokine Release Syndrome diagnosis due to chimeric antigen receptor-T cell therapy

Initial Approval:

4 months

Renewal:

1 year
Requires:
Member has shown improvement in signs and symptoms of disease

Dosing and administration:

- **Humira:**
  - For Hidradenitis suppurativa:
    - Adults: 160 mg day 1, followed by 80 mg day 15(6 syringes/28 days) for induction period, thereafter 40 mg once a week starting day 29 (4 syringes/28 days)
    - Children 12-17 years old:
      - >60 kg or more: 160 mg day 1, followed by 80 mg day 15(6 syringes/28 days) for induction period, thereafter 40 mg once a week starting day 29 (4 syringes/28 days)
      - 30-59 kg: 80 mg on day 1, then maintenance treatment of 40 mg once every other week starting on day 8.
  - For Rheumatoid Arthritis , Ankylosing Spondylitis , Psoriatic Arthritis , and Juvenile Idiopathic Arthritis : Two syringes/pens per 28 days
  - For Crohn's, Ulcerative Colitis:
    - Six syringes/pens in the initial 28 days
      Crohn's, Ulcerative Colitis: Two syringes/pens per 28 days after induction period;
  - For Psoriasis
    - Four syringes/pens in the initial 28 days
    - Two syringes/pens per 28 days after induction period
  - For Uveitis:
    - Adults: 80 mg day 1, followed by 40 mg dose every other week starting 1 week after the initial dose(4 syringes in the initial 28 days), then 2 syringes/ pens per days after induction perioid.
    - Children 2-17 years old:
      - 30 kg or more: 40 mg every other week
      - 15-29 kg: 20 mg every other week
      - 10-14 kg: 10 mg every other week
- **Enbrel**
  - For Rheumatoid Arthritis , Ankylosing Spondylitis , Psoriatic Arthritis, and Juvenile Idiopathic Arthritis: Four, 50mg syringes, OR eight 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 Subcutaneous**
  - For Rheumatoid Arthritis:
    - Weight <100kg: Two syringes per 28 days. Max dose is 4 syringes per 28 days

        - Weight ≥100kg: Four syringes per 28 days
    - For Giant Cell Arteritis:
        - 162mg once weekly in combination with a tapering course of glucocorticoids

      162mg once every other week in combination with a tapering course of glucocorticoids may be prescribed based on clinical presentation.
- **Actemra intravenous**
    - For Rheumatoid Arthritis : 4 to 8mg/kg every 28 days
    - For Polyarticular Juvenile Idiopathic Arthritis :
        - Weight <30kg: 10mg/kg every 28 days
        - Weight ≥30kg: 8mg/kg every 28 days
    - For Systemic Juvenile Idiopathic Arthritis:
        - Weight <30kg: 12mg/kg every 14 days
        - Weight ≥30kg: 8mg/kg every 14 days
    - For Cytokine Release Sydrome:
        - 30 kg or more: 8 mg/kg for one dose, up to 3 additional doses if no clinical improvement (max dose 800 mg)
        - Less than 30 kg: 12 mg/kg for one dose, up to 3 additional doses If no clinical improvement (max dose 800 mg)
- **Cimzia**
    - Six syringes/vials allowed in the initial 54 days
    - Two syringes/vials per 28 days after induction period
- **Cosentyx**
    - For Ankylosing Spondylitis and Psoriatic Arthritis:
        - Four syringes/pens in the initial 28 days
        - One syringe/pen per 28 days after induction period
    - For Psoriasis
        - Eight syringes/pens in the initial 28 days
        - Two syringes/pens per 28 days after induction period
- **Entyvio**
    - For Crohns and Ulcerative Colitis: 300 mg at weeks 0, 2 and 6 for induction (3 vials/6 weeks), then 300 mg (1 vial) every 8 weeks after the induction period
- **Ilaris**
    - For Cryopyrin-Associated Periodic Syndromes (>40 kg): 150mg every 8 weeks, one vial per 56 days
    - For Cryopyrin-Associated Periodic Syndromes (≤40 kg): 2mg/kg every 8 weeks, one vial per 56 days Dose may be increased to 3mg/kg given every 8 weeks
    - For Systemic Juvenile Idiopathic Arthritis : 4mg/kg (max 300mg) every 4 weeks
        - QLL for doses <180mg: One vial per 28 days
        - QLL for doses >180mg: Two vials per 28 days
- **Ilumya**
    - For Plaque Psoriasis: 100 mg (two syringes) per 28 days for the induction period; then 100 mg (one syringe) every 12 weeks after the induction period.
- **Kevzara**
    - For Rheumatoid Arthritis : 200mg SC every 2 weeks, two syringes per 28 days

- **Kineret**
  - For Rheumatoid Arthritis , Juvenile Idiopathic Arthritis, and Cryopyrin-Associated Periodic Syndromes : One syringe per day
- **Olumiant**
  - For Rheumatoid Arthritis: One tablet (2mg) daily
- **Orencia IV:**
  - For Rheumatoid Arthritis :
    - Weight <60kg: Two vials per 28 days
    - Weight 60-100kg: Three vials per 28 days
    - Weight >100kg: Four vials per 28 days
  - For Juvenile Idiopathic Arthritis :
    - Weight <75kg: 10mg/kg every 28 days
    - Weight >75kg: Follow adult Rheumatoid Arthritis dosing above
- **Orencia Subcutaneous**
  - For Rheumatoid Arthritis : 125 mg once a week
  - For Polyarticular juvenile idiopathic arthritis:
    - Children and adolescents 2 years and older weighing greater 50 kg: 125 mg subcutaneously once a week
    - Children and adolescents 2 years and older weighing 25 kg to less than 50 kg: 87.5 mg subcutaneously once a week
    - Children and adilesents 2 years and older weighing 10kg to 25 kg: 50 mg subcutaneously once a week
  - For Psoriatic Arthritis: 125 mg subcutaneously once a week

- **Remicade/Inflectra/Renflexis**
  - For Rheumatoid Arthritis: 3mg/kg at week 0, 2 and 6, then every 8 weeks thereafter. Max dose 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 10mg/kg every 8 weeks
  - For Ulcerative Colitis, Psoriatic Arthritis, and Psoriasis: 5mg/kg at week 0, 2 and 6, then every 8 weeks thereafter.
  - For Ankylosing Spondylitis: 5mg/kg at week 0, 2 and 6, then every 6 weeks thereafter.
- **Siliq**
  - For psoriasis: Four (210mg) syringes for first 28 days; Two syringes per 28 days thereafter.
  - Treatment should be discontinued if inadequate response after 12 to 16 weeks.

- **Simponi**
  - For Rheumatoid Arthritis, Ankylosing Spondylitis, and Psoriatic Arthritis : One, 50mg syringe per 28 days
  - For Ulcerative Colitis:
    - Three, 100mg syringes allowed in the initial 54 days
    - One, 100mg syringe per 28 days after induction period
- **Simponi Aria**

  - For Rheumatoid Arthritis : 2mg/kg at week 0 and 4, then every 8 weeks thereafter
- **Stelara**
  - For Psoriasis
    - Weight ≤100kg: One, 45mg syringe per 28 days for initial 2 months; then one, 45mg syringe per 84 days
    - Weight >100kg: One, 90mg syringe per 28 days for initial 2 months; then one, 90mg syringe per 84 days
  - For Psoriatic Arthritis
    - One, 45mg syringe per 28 days for initial 2 months; then 1, 45mg syringe per 84 days
  - For Crohns
    - One, 90mg syringe per 56 days
- **Taltz**
  - For Psoriasis
    - Three syringes in the first 28 days
    - Two syringes per 28 days for months 2 and 3
    - One syringe per 28 days after initial induction
  - For Psoriatic Arthritis
    - 160 mg subcutaneously at week 0 (administered as two 80-mg injections, 2 syringes/2 ml); then 80 mg subcutaneously,1 syringe(1 ml) every 4 weeks.
- **Tremfya**
  - For psoriasis
    - 100mg SQ at week 0 and week 4, followed by 100mg every 8 weeks.
- **Tysabri**
  - For Crohns: 1 vial per 28 days
- **Xeljanz**
  - For Rheumatoid Arthritis: Two (5 mg) tablets per day
  - For Psoriatic Arthritis: Two (5 mg) tablets per day
  - For Ulcerative Colitis: 10 mg twice a day for 8 weeks, then 5 mg or 10 mg twice a day
- **Xeljanz XR**
  - For Rheumatoid Arthritis: One (11 mg) tablet per day
  - For Psoriatic Arthritis: One (11 mg) tablet per day

Examples of Contraindications to Methotrexate

- Alcoholism, alcoholic liver disease or other chronic liver disease
- Breastfeeding
- Blood dyscrasias (for example thrombocytopenia, leukopenia, significant anemia)
- Elevated liver transaminases
- History of intolerance or adverse event
- Hypersensitivity
- Interstitial pneumonitis or clinically significant pulmonary fibrosis
- Myelodysplasia

- Pregnancy or planning pregnancy (male or female)
- Renal impairment
- Significant drug interaction

Examples of Clinical Reasons to Avoid Treatment with Methotrexate, Cyclosporine:

- Alcoholism, alcoholic liver disease or other chronic liver disease
- Breastfeeding
- Drug interaction
- Cannot be used due to risk of treatment-related toxicity
- Pregnancy or planning pregnancy (male or female)
- Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

Examples of Contraindications to the Use of NSAIDs:

- Allergic-type reaction following aspirin or other NSAID administration
- Asthma
- Gastrointestinal bleeding
- History of intolerance or adverse event
- Urticaria
- Significant drug interaction

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