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)
Skyrizi (risankizumab)
Taltz (ixekizumab)
Tremfya (guselkumab)
Tysabri (natalizumab)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib)
Otezla (apremilast)

Preferred Agents: ENBREL HUMIRA, CIMZIA, XELJANZ, XELJANZ XR

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

Non-Preferred Cytokines and Cell Adhesion Molecule (CAM) Antagonists:
Require trial and failure of Enbrel, Humira, Cimzia, Xeljanz, or Xeljanz XR where indicated, in addition to all other clinical criteria.

NOTE: 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.
- Prescribed dose is Food and Drug Administration (FDA) approved for indication. Doses above Food and Drug Administration (FDA) approved labeling will not be authorized. Quantity limits exist.
- Anti-Tumor Necrosis Factors only: Member does not have New York Heart Association (NYHA) class III or IV Congestive Heart Failure.
- 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.
- 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, Cimzia, Xeljanz, Xeljanz XR**, Actemra, Inflectra, Kevzara, Kineret, Olumiant, Orencia, Remicade, Renflexis, Simponi, Simponi Aria,
  - 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 methotrexate. If there is an intolerance or contraindication to methotrexate, member can use sulfasalazine, leflunomide or hydroxychloroquine
  - Medication will be used concurrently with methotrexate or another non-biologic disease-modifying antirheumatic drug (DMARD) such as sulfasalazine, leflunomide, or hydroxychloroquine
- **Systemic Juvenile Idiopathic Arthritis: Enbrel, Humira,** Orencia (subcutaneous/intravenous)
  - Member is 2 years of age or older - Enbrel, Humira, 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
  - Note: Member does not require trial of formulary agents
- **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)
  - Note: Member does not require trial of formulary agents

- **Polyarticular Juvenile Idiopathic Arthritis:** Enbrel, Humira, Orencia (intravenous/subcutaneous), Actemra
  - Member is 2 years of age or older - Enbrel, Humira, Orencia (subcutaneous), 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 leflunomide or sulfasalazine 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 2 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 3 months trial of methotrexate
  - If member has an intolerance, or contraindication to methotrexate, a documented trial of leflunomide or sulfasalazine for 3 months is required
- **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 formulary agents
- **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)
  - NOTE: Member does not require trial of formulary agents
- **Familial Mediterranean Fever:** Ilaris
  - Member is 2 years of age or older
  - Documented inadequate response, intolerance, or contraindication to colchicine at maximum indicated dose (Claims history to support compliance or adherence).
  - NOTE: Member does not require trial of formulary agents
- **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
- NOTE: Member does not require trial of formulary agents

- **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, Xeljanz, Xeljanz XR,** Cosentyx, Inflectra, Orencia, Otezla, Remicade, Renflexis, Simponi, Simponi Aria, Stelara, Taltz
  - 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, there was a three months trial of sulfasalazine, or leflunomide
    - Member has predominantly axial disease or active enthesitis/dactylitis, and inadequate response to 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 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, Otezla, Remicade, Renflexis, Siliq, Tremfya, Stelara, Taltz, Skyrizi
  - Member is 18 years of age or older - **Humira, Cimzia**, Cosentyx, Ilumya, Inflectra, Remicade, Renflexis, Siliq, Skyrizi, 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 ultraviolet 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, Xeljanz,** Entyvio, Inflectra, Remicade, Renflexis, Simponi, Stelara
  - Member is 18 years of age or older - **Humira**, **Xeljanz,** Entyvio, Inflectra, Simponi, Renflexis
  - Member is 6 years of age or older - Remicade
  - Steroid Dependent:
    - 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
  - Steroid Refractory:
    - 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
- **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
- **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)
- **Uveitis: Humira**

- Member is 2 years of age or older
- Intermediate, posterior, or pan uveitis is not caused by infection
- Documented inadequate response, or intolerable side effect, with any of the following:
  - Corticosteroids, methotrexate, azathioprine, mycophenolate, cyclosporine, tacrolimus, or medications are not appropriate

- **Oral Ulcers Associated with Behçet's Disease:** Otezla
  - Diagnosis of Behçet's disease with active recurrent oral ulcers
  - Age is 18 years or older
  - Documentation of previous trial and failure with at least one Non-Biologic Disease-Modifying Anti-Rheumatic Drug such as methotrexate, leflunomide, sulfasalazine or hydroxychloroquine

- **Cytokine Release Syndrome:** Actemra Intravenous Only
  - Member is 2 years of age or older
  - Member has Grade three or four of severe or life-threatening diagnosis due to chimeric antigen receptor-T cell therapy
  - NOTE: Member does not require trial of formulary agents

Initial Approval: 6 months

Renewal Approval: 6 months

- Requires: Documentation indicating member has shown improvement in signs and symptoms of disease

Dosing and administration:

- **Humira:**
  - 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.
  - Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis, and Juvenile Idiopathic Arthritis:
    - Two syringes/pens per 28 days
  - Crohn's, Ulcerative Colitis:
    - Six syringes/pens in initial 28 days
    - Crohn's, Ulcerative Colitis: Two syringes/pens per 28 days after induction period
  - Psoriasis

        - Four syringes/pens in the initial 28 days
        - Two syringes/pens per 28 days after induction period
    - 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 period.
        - 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**
    - Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis, and Juvenile Idiopathic Arthritis:
        - Four, 50mg syringes, OR eight 25mg syringes per 28 days
    - Psoriasis:
        - 8, 50mg syringes per 28 days for the initial 3 months
        - 4, 50mg syringes per 28 days after induction period
- **Actemra Subcutaneous**
    - Rheumatoid Arthritis:
        - Weight <100kg: Two syringes per 28 days. Max dose is 4 syringes per 28 days
        - Weight ≥100kg: Four syringes per 28 days
    - 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**
    - Rheumatoid Arthritis: 4 to 8mg/kg every 28 days
    - Polyarticular Juvenile Idiopathic Arthritis:
        - Weight <30kg: 10mg/kg every 28 days
        - Weight ≥30kg: 8mg/kg every 28 days
    - Systemic Juvenile Idiopathic Arthritis:
        - Weight <30kg: 12mg/kg every 14 days
        - Weight ≥30kg: 8mg/kg every 14 days
    - Cytokine Release Syndrome:
        - 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**
  - Ankylosing Spondylitis and Psoriatic Arthritis:
    - Four syringes/pens in the initial 28 days
    - One syringe/pen per 28 days after induction period
  - Psoriasis
    - Ten syringes/pens in the initial 28 days
    - Two syringes/pens per 28 days after induction period
- **Entyvio**
  - Crohns and Ulcerative Colitis:
    - 300 mg at weeks 0, 2, 6 for induction (3 vials/6 weeks), then 300 mg (1 vial) every 8 weeks after induction period
- **Ilaris**
  - Cryopyrin-Associated Periodic Syndromes (>40 kg):
    - 150mg every 8 weeks, one vial per 56 days
  - 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
  - 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**
  - 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**
  - Rheumatoid Arthritis:
    - 200mg SC every 2 weeks, two syringes per 28 days
- **Kineret**
  - Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, and Cryopyrin-Associated Periodic Syndromes:
    - One syringe per day
- **Olumiant**
  - Rheumatoid Arthritis:
    - One tablet (2mg) daily
- **Orencia IV:**
  - Rheumatoid Arthritis:
    - Weight <60kg: Two vials per 28 days
    - Weight 60-100kg: Three vials per 28 days
    - Weight >100kg: Four vials per 28 days

  - Juvenile Idiopathic Arthritis:
    - Weight <75kg: 10mg/kg every 28 days
    - Weight >75kg: Follow adult Rheumatoid Arthritis dosing above
- **Orencia Subcutaneous**
  - Rheumatoid Arthritis:
    - 125 mg once a week
  - 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 adolescents 2 years and older weighing 10kg to 25 kg: 50 mg subcutaneously once a week
  - Psoriatic Arthritis:
    - 125 mg subcutaneously once a week
- **Remicade/Inflectra/Renflexis**
  - 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.
  - Crohns:
    - 5mg/kg at week 0, 2, 6, then every 8 weeks thereafter. Max dose 10mg/kg every 8 weeks
  - Ulcerative Colitis, Psoriatic Arthritis, Psoriasis:
    - 5mg/kg at week 0, 2, 6, then every 8 weeks thereafter
  - Ankylosing Spondylitis:
    - 5mg/kg at week 0, 2, 6, then every 6 weeks thereafter
- **Siliq**
  - 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**
  - Rheumatoid Arthritis, Ankylosing Spondylitis, and Psoriatic Arthritis:
    - One, 50mg syringe per 28 days
  - Ulcerative Colitis:
    - Three, 100mg syringes allowed in the initial 54 days
    - One, 100mg syringe per 28 days after induction period
- **Simponi Aria**
  - Rheumatoid Arthritis:
    - 2mg/kg at week 0 and 4, then every 8 weeks thereafter
- **Skyrizi**
  - Plaque psoriasis:

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