Reference number(s)
1959-A

Specialty Guideline Management Actemra and Biosimilars

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Actemra	tocilizumab
Avtozma	tocilizumab-anoh
Tofidence	tocilizumab-bavi
Tyenne	tocilizumab-aazq
tocilizumab-aazg (unbranded Tyenne)	tocilizumab-aazg
tocilizumab-anoh (unbranded Avtozma)	tocilizumab-anoh

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1-6]

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs)
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (pJIA)
- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis (sJIA)
- Adult patients with giant cell arteritis (GCA)
- Adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for slowing the rate of decline in pulmonary function

- Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS)
- Hospitalized adult patients with coronavirus disease 2019 (COVID-19) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)

Compendial Uses[7,20]

- Unicentric Castleman disease
- Multicentric Castleman disease
- Oligoarticular juvenile idiopathic arthritis
- Immune checkpoint inhibitor-related toxicity
- Acute graft versus host disease
- Cytokine release syndrome (other than severe or life-threatening CAR T cell-induced CRS)
- Polymyalgia rheumatica
- Moderate to severe rheumatoid arthritis with no previous treatment failure

Note: The criteria outlined in this policy is only applicable to coverage in the outpatient setting. Hospitalized members receiving treatment for COVID-19 will be managed according to the member's inpatient benefit.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Rheumatoid arthritis (RA)

Initial requests

- Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable).
- Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).

Continuation requests

Chart notes or medical record documentation supporting positive clinical response.

Articular juvenile idiopathic arthritis

Initial requests

Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.

Continuation requests

Chart notes or medical record documentation supporting positive clinical response.

Systemic juvenile idiopathic arthritis (sJIA)

Initial requests

Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable).

Continuation requests

Chart notes or medical record documentation supporting positive clinical response.

Immune checkpoint inhibitor-related toxicity, and acute graft versus host disease (initial requests only)

Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

Giant cell arteritis (GCA)

Continuation requests

Chart notes or medical record documentation supporting positive clinical response.

Systemic sclerosis-associated interstitial lung disease (SSc-ILD)

Initial requests

Result of a chest high-resolution computed tomography (HRCT) study.

Polymyalgia rheumatica and immune checkpoint inhibitor-related inflammatory arthritis

Initial requests

Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

Continuation requests

Chart notes or medical record documentation supporting positive clinical response.

Prescriber Specialties

This medication must be prescribed by or in consultation with one of the following:

- Rheumatoid arthritis, articular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, giant cell arteritis, and polymyalgia rheumatica: rheumatologist
- Systemic sclerosis-associated interstitial lung disease: rheumatologist or pulmonologist
- Immune checkpoint inhibitor-related inflammatory arthritis: oncologist, hematologist, or rheumatologist
- Cytokine release syndrome, unicentric Castleman disease, multicentric Castleman disease, acute graft versus host disease, and immune checkpoint inhibitor-related toxicity: oncologist or hematologist

Coverage Criteria

Rheumatoid arthritis (RA)[1-6,8,9,16,18-20]

Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when either of the following criteria is met:

- Member has been tested for either of the following biomarkers and the test was positive:
  - Rheumatoid factor (RF)
  - Anti-cyclic citrullinated peptide (anti-CCP)
- Member has been tested for ALL of the following biomarkers:
  - RF
  - Anti-CCP
  - C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)

Articular juvenile idiopathic arthritis[1-6,12,21]

Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic or targeted synthetic drug (e.g., Xeljanz) indicated for active articular juvenile idiopathic arthritis.

Authorization of 12 months may be granted for members 2 years of age or older for treatment of active articular juvenile idiopathic arthritis when any of the following criteria is met:

- Member has had an inadequate response to methotrexate or another conventional synthetic drug (e.g., leflunomide, sulfasalazine, hydroxychloroquine) administered at an adequate dose and duration.
- Member has had an inadequate response to a trial of scheduled non-steroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids (e.g., triamcinolone hexacetonide) and one of the following risk factors for poor outcome:

  - Involvement of ankle, wrist, hip, sacroiliac joint, and/or temporomandibular joint (TMJ)
  - Presence of erosive disease or enthesitis
  - Delay in diagnosis
  - Elevated levels of inflammation markers
  - Symmetric disease
- Member has risk factors for disease severity and potentially a more refractory disease course (see Appendix B) and the member also meets one of the following:
  - High-risk joints are involved (e.g., cervical spine, wrist, or hip)
  - High disease activity
  - Is judged to be at high risk for disabling joint disease

Systemic juvenile idiopathic arthritis (sJIA)[1-6,11,21]

Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic indicated for active sJIA.

Authorization of 12 months may be granted for members 2 years of age or older for treatment of active sJIA when the member has active systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis).

Giant cell arteritis (GCA)[1-6,13]

Authorization of 12 months may be granted for adult members for treatment of giant cell arteritis when the member's diagnosis was confirmed by either of the following:

- Temporal artery biopsy or cross-sectional imaging
- Acute-phase reactant elevation (i.e., high erythrocyte sedimentation rate [ESR] and/or high serum C-reactive protein [CRP]).

Systemic sclerosis-associated interstitial lung disease (SSc-ILD)[1,17,23,24]

Authorization of 12 months may be granted for adult members for treatment of sclerosis-associated interstitial lung disease when the diagnosis was confirmed by a high-resolution computed tomography (HRCT) study of the chest.

Cytokine release syndrome[1,7]

Authorization of 1 month may be granted for the prophylaxis or treatment of cytokine release syndrome (CRS).

Unicentric Castleman disease[7]

Authorization of 12 months may be granted for treatment of unicentric Castleman disease when all of the following criteria are met:

- The member is human immunodeficiency virus (HIV)-negative.
- The member is human herpesvirus-8-negative.

- The requested medication will be used as a single agent.
- The disease has progressed following treatment of relapsed/refractory disease or has surgically unresectable disease.

Multicentric Castleman disease[7]

Authorization of 12 months may be granted for treatment of multicentric Castleman disease when either of the following criteria is met:

- The member meets both of the following:
  - The requested medication will be used as a single agent.
  - The disease has progressed following treatment of relapsed/refractory or progressive disease.
- The requested medication is being used as a substitute for siltuximab when there is a shortage of siltuximab or it is not available.

Immune checkpoint inhibitor-related toxicity[7]

Authorization of 12 months may be granted for treatment of immune checkpoint inhibitor-related toxicity when the member has moderate or severe immunotherapy-related inflammatory arthritis and either of the following criteria is met:

- Member has had an inadequate response to corticosteroids or a conventional synthetic drug (e.g., methotrexate, sulfasalazine, leflunomide, hydroxychloroquine).
- Member has an intolerance or contraindication to corticosteroids and a conventional synthetic drug (e.g., methotrexate, sulfasalazine, leflunomide, hydroxychloroquine).

Authorization of 6 months may be granted for treatment of immune checkpoint inhibitor-related toxicity when either of the following criteria is met:

- Member has had an inadequate response to systemic corticosteroids.
- Member has an intolerance or contraindication to corticosteroids.

Acute graft versus host disease[7]

Authorization of 12 months may be granted for treatment of acute graft versus host disease when either of the following criteria is met:

- Member has had an inadequate response to systemic corticosteroids.
- Member has an intolerance or contraindication to corticosteroids.

Polymyalgia rheumatica (PMR)[7]

Authorization of 12 months may be granted for treatment of polymyalgia rheumatica (PMR) when any of the following criteria is met:

- Member has had an inadequate response to systemic corticosteroids.
- Member has had a disease flare during a taper with systemic corticosteroids.
- Member has had an inadequate response to methotrexate.

- Member has had an intolerance or contraindication to both systemic corticosteroids and methotrexate (see Appendix A).

Continuation of Therapy

Rheumatoid arthritis (RA)[1-6,8,9,16,18-19]

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active RA and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

Articular juvenile idiopathic arthritis[1-6,12,21]

Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

- Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
- Number of joints with limitation of movement
- Functional ability

Systemic juvenile idiopathic arthritis (sJIA)[1-6,11,21]

Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for sJIA and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

- Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
- Number of joints with limitation of movement
- Functional ability
- Systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis)

Giant cell arteritis (GCA)[1,14]

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for GCA and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

- Headaches
- Scalp tenderness
- Tenderness and/or thickening of superficial temporal arteries

- Constitutional symptoms (e.g., weight loss, fever, fatigue, night sweats)
- Jaw and/or tongue claudication
- Acute visual symptoms (e.g., amaurosis fugax, acute visual loss, diplopia)
- Symptoms of polymyalgia rheumatica (e.g., shoulder and/or hip girdle pain)
- Limb claudication

Systemic sclerosis-associated interstitial lung disease (SSc-ILD)[1]

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for SSc-ILD when the member is currently receiving treatment with Actemra or Tyenne.

Immune checkpoint inhibitor-related inflammatory arthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for immunotherapy-related inflammatory arthritis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition.

Cytokine release syndrome, acute graft versus host disease, and immune checkpoint inhibitor-related toxicity

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

Unicentric Castleman disease and Multicentric Castleman disease

Authorization of 12 months may be granted for continued treatment in members (including new members) who are using the requested medication for Unicentric Castleman disease or Multicentric Castleman disease when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Polymyalgia rheumatica (PMR)

Authorization of 12 months may be granted for continued treatment in members who are using the requested medication for PMR and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

- Morning stiffness
- Hip or shoulder pain
- Hip or shoulder range of motion
- C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)

Other[1-6,15]

For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [TST] or an interferon-release assay [IGRA]) within 12 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

If the screening testing for TB is positive, there must be further testing to confirm there is no active disease (e.g., chest x-ray). Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Appendix

Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate[22]

- Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
- Drug interaction
- Risk of treatment-related toxicity
- Pregnancy or currently planning pregnancy
- Breastfeeding
- Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
- Hypersensitivity
- History of intolerance or adverse event

Appendix B: Risk Factors for Articular Juvenile Idiopathic Arthritis[21]

- Positive rheumatoid factor
- Positive anti-cyclic citrullinated peptide antibodies
- Pre-existing joint damage

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