AETNA BETTER HEALTH®
Coverage Policy/Guideline

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Effective Date:	2/1/2024	Last Review Date:	11/2023

Applies to:	☐Illinois	☐Florida	☒Florida Kids
	☐New Jersey	☐Maryland	☐Michigan
	☒Pennsylvania Kids	☐Virginia	☐Kentucky PRMD

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for Actemra under the patient's prescription drug benefit.

Description:

A. FDA-Approved Indications
   1. 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).
   2. Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
   3. Patients 2 years of age and older with active systemic juvenile idiopathic arthritis (sJIA).
   4. Adult patients with giant cell arteritis (GCA).
   5. Adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for slowing the rate of decline in pulmonary function.
   6. 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).
   7. 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).

B. Compendial Uses
   1. Unicentric Castleman disease
   2. Multicentric Castleman disease
   3. Oligoarticular juvenile idiopathic arthritis
   4. Immune checkpoint inhibitor-related toxicities - inflammatory arthritis
   5. Acute graft versus host disease
   6. Cytokine release syndrome (other than severe or life-threatening CAR T cell-induced CRS)

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

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

Applicable Drug List:

Non-preferred: Actemra, Tofidence

Policy/Guideline:

Documentation for all indications:
The patient is unable to take a preferred adalimumab product, Enbrel and Rinvoq, where indicated, for the given diagnosis due to a trial and inadequate treatment response or intolerance, or a contraindication. Documentation is required for approval.

Documentation:

A. **Rheumatoid arthritis (RA)**
   1. Initial requests:
      i. 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.
      ii. 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).
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. **Articular juvenile idiopathic arthritis**
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. **Systemic juvenile idiopathic arthritis (sJIA)**
   1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.
   2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D. **Cytokine release syndrome, immune checkpoint inhibitor-related toxicity, and acute graft versus host disease:** For 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.

E. **Giant cell arteritis (GCA):** For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

F. **Systemic sclerosis-associated interstitial lung disease (SSc-ILD):** For initial requests: Result of a chest high-resolution computed tomography (HRCT) study.

Prescriber Specialty:
This medication must be prescribed by or in consultation with one of the following:
A. Rheumatoid arthritis, articular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, and giant cell arteritis: rheumatologist
B. Systemic sclerosis-associated interstitial lung disease: rheumatologist or pulmonologist
C. Immune checkpoint inhibitor-related toxicity: oncologist, hematologist, or rheumatologist
D. Cytokine release syndrome, unicentric Castleman disease, multicentric Castleman disease, and acute graft versus host disease: oncologist or hematologist

Criteria for Initial Approval:
A. Rheumatoid arthritis (RA)
1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following criteria are met:
   i. Member meets either of the following criteria:
      a. Member has been tested for either of the following biomarkers and the test was positive:
         1. Rheumatoid factor (RF)
         2. Anti-cyclic citrullinated peptide (anti-CCP)
      b. Member has been tested for ALL of the following biomarkers:
         1. RF
         2. Anti-CCP
         3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
   ii. Member meets either of the following criteria:

a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Articular juvenile idiopathic arthritis

1. 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 indicated for active articular juvenile idiopathic arthritis.

2. 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:
   i. 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.
   ii. 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:
      a. Involvement of ankle, wrist, hip, sacroiliac joint, and/or temporomandibular joint (TMJ)
      b. Presence of erosive disease or enthesitis
      c. Delay in diagnosis
      d. Elevated levels of inflammation markers
      e. Symmetric disease
   iii. 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:
      a. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
      b. High disease activity.
      c. Is judged to be at high risk for disabling joint disease.

C. Systemic juvenile idiopathic arthritis (sJIA)

1. 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.

2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of active sJIA when both of the following criteria are met:

i. Member has active systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis).
ii. Member has had an inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs) or systemic glucocorticoids.

D. Giant cell arteritis (GCA)

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

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

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

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.

F. Cytokine release syndrome

1. Authorization of 1 month may be granted for members 2 years of age or older for treatment of chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS).
2. Authorization of 1 month may be granted for treatment of cytokine release syndrome in members with refractory CRS related to blinatumomab therapy.

G. Unicentric Castleman disease

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

1. The member is HIV-negative.
2. The member is human herpesvirus-8-negative.
3. The requested medication will be used as a single agent.
4. The disease has progressed following treatment of relapsed/refractory disease.

H. Multicentric Castleman disease

Authorization of 12 months may be granted for treatment of multicentric Castleman disease when both of the following are met:

1. The requested medication will be used as a single agent.
2. The disease has progressed following treatment of relapsed/refractory or progressive disease.

I. Immune checkpoint inhibitor-related toxicity

Authorization of 12 months may be granted for treatment of immune checkpoint inhibitor-related toxicity when then member has severe immunotherapy-related inflammatory arthritis and meets either of the following:

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

J. Acute graft versus host disease

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

1. Member has experienced an inadequate response to systemic corticosteroids.
2. Member has an intolerance or contraindication to corticosteroids.

Continuation of Therapy:

A. Rheumatoid arthritis (RA)

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.

B. Articular juvenile idiopathic arthritis

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:

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

C. Systemic juvenile idiopathic arthritis (sJIA)

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:

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

D. Giant cell arteritis (GCA)

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:

1. Headaches
2. Scalp tenderness
3. Tenderness and/or thickening of superficial temporal arteries
4. Constitutional symptoms (e.g., weight loss, fever, fatigue, night sweats)
5. Jaw and/or tongue claudication
6. Acute visual symptoms (e.g., amaurosis fugax, acute visual loss, diplopia)
7. Symptoms of polymyalgia rheumatica (e.g., shoulder and/or hip girdle pain)
8. Limb claudication

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

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.

F. Immune checkpoint inhibitor-related toxicity

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.

G. Cytokine release syndrome and acute graft versus host disease

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

H. All other diagnoses

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in criteria for initial approval when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Other Criteria:

Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 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. 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.

Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug for the same indication.

Appendix A: Examples of clinical reasons to avoid pharmacologic treatment with methotrexate

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

Appendix B: Risk factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor

2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

Approval Duration and Quantity Restrictions:

Approval:

Initial Approval: 1 month for Cytokine Release Syndrome, 12 months for all other indications
Renewal Approval: 1 month for Cytokine Release Syndrome, 12 months for all other indications

Quantity Level Limit:

- Actemra (tocilizumab) 162 mg per 0.9 mL prefilled syringe for subcutaneous injection: 4 syringes per 28 days
- Actemra (tocilizumab) 162 mg per 0.9 mL ACTPen autoinjector for subcutaneous injection: 4 autoinjectors per 28 days
- Actemra (tocilizumab) 80 mg per 4 mL single-use vial: 40 mL (10 vials) per 14 days
- Actemra (tocilizumab) 200 mg per 10 mL single-use vial: 40 mL (4 vials) per 14 days
- Actemra (tocilizumab) 400 mg per 20 mL single-use vial: 40 mL (2 vials) per 14 days

References:

1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; December 2022.
2. Tofidence [package insert]. Cambridge, MA: Biogen MA Inc.; September 2023.
3. The NCCN Drugs & Biologics Compendium. © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed October 10, 2023.
4. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
5. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. *Ann Rheum Dis.* 2020;*79*:685-699.
6. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
7. 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 & Rheumatism.* 2013;65:2499-2512.
8. Ringold S, Angeles-Han S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *American College of Rheumatology*. 2019;1-18.
9. Stone JH, Tuckwell K, Dimonaco S, et al. Efficacy and safety of tocilizumab in patients with giant cell arteritis: Primary and secondary outcomes from a phase 3, randomized, double-blind, placebo-controlled trial. 2016 ACR/ARHP Annual meeting. Abstract number 911.
10. Hellmich B, Agueda A, Monti S, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis*. 2020;79(1):19-30.

11. Testing for TB Infection. Centers for Disease Control and Prevention. Retrieved on January 4, 2023 from: https://www.cdc.gov/tb/topic/testing/tbtesttypes.htm.
12. Aletaha D, Neogi T, Silman, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum*. 2010;62(9):2569-81.
13. Khanna D, Lin CJF, Furst DE, et al. Tocilizumab in systemic sclerosis: a randomised, double-blind, placebo-controlled, phase 3 trial. [published correction appears in Lancet Respir Med. 2020 Oct;8(10):e75] [published correction appears in Lancet Respir Med. 2021 Mar;9(3):e29]. *Lancet Respir Med*. 2020;8(10):963-974. doi:10.1016/S2213-2600(20)30318-0.
14. Smolen JS, Aletaha D. Assessment of rheumatoid arthritis disease activity and physical function. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available with subscription. URL: www.uptodate.com. Accessed January 4, 2023.
15. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthrit Care Res*. 2021;0:1-16.
16. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed January 4, 2023.
17. Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for oligoarthritis, temporomandibular joint arthritis, and systemic juvenile idiopathic arthritis. *Arthritis Rheumatol*. 2022;74(4):553-569.
18. Menter A, Gelfand JM, Connor C, et al. Joint AAD-NPF guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol.* 2020;82(6): 1445-86.