PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Actemera Subcutaneous Prior Authorization Policy
- Actemra® (tocilizumab subcutaneous injection – Genentech/Roche)

REVIEW DATE: 03/31/2021

OVERVIEW

Actemra subcutaneous injection, an interleukin-6 (IL-6) receptor inhibitor, is approved for the following uses:[1]

- **Giant cell arteritis** in adults.
- **Interstitial lung disease associated with systemic sclerosis,** for slowing the rate of decline in pulmonary function in adults.
- **Polyarticular juvenile idiopathic arthritis**, for the treatment of active in patients 2 years of age and older.
- **Rheumatoid arthritis**, for treatment of adults with moderate to severe active disease who have had an inadequate response to one or more disease modifying antirheumatic drugs (DMARDs).
- **Systemic juvenile idiopathic arthritis**, for the treatment of active disease in patients two years of age and older.

Guidelines/Clinical Efficacy

Il-6 blockers are mentioned in multiple guidelines for treatment of inflammatory conditions. Clinical data also support use of Actemra in other conditions.

- **Giant Cell Arteritis and Polymyalgia Rheumatica:** Recommendations from the European League Against Rheumatism (EULAR) [2018] state the diagnosis of giant cell arteritis may be made without biopsy if there is a high suspicion of giant cell arteritis and a positive imaging test.[4] In the pivotal trial evaluating Actemra subcutaneous for giant cell arteritis (n = 251), patients were treated with corticosteroids in an open-label fashion (20 mg to 60 mg/day) during the screening period prior to treatment with Actemra subcutaneous.[2-3] Sustained remission at Week 52 was achieved in 56% of patients who received Actemra subcutaneous every week + 26-week prednisone taper and 53% of patients who received Actemra every other week + 26-week prednisone taper vs. in 14% of patients in the 26-week prednisone taper and 18% of patients in the 52-week prednisone taper. This trial allowed patients with polymyalgia rheumatica and evidence of large-vessel vasculitis by angiography or imaging (e.g., magnetic resonance imaging [MRI], computed tomography angiography [CTA], positron emission tomography – computed tomography [PET/CT]) to be included in the study. Additional small studies and/or case reports support use of Actemra in patients with polymyalgia rheumatica without documented symptoms of giant cell arteritis.[5-7]
- **Interstitial Lung Disease Associated with Systemic Sclerosis:** EULAR guidelines for systemic sclerosis (2016) recommend consideration of cyclophosphamide for treatment of interstitial lung disease associated with systemic sclerosis.[14] Additionally, hematopoietic stem cell transplantation should be considered for selected patients with rapidly progressive disease at risk of organ failure. In the pivotal trial evaluating Actemra subcutaneous for systemic sclerosis-associated interstitial lung disease, patients were required to have a percentage of predicted forced vital capacity (FVC% predicted) > 55%.[15] Among patients with ILD confirmed on high-resolution computed tomography scan (n = 136), the change from baseline in FVC% predicted at Week 48 was significantly improved in the group taking Actemra (0.07 vs. -6.40 with placebo).

- **Polyarticular Juvenile Idiopathic Arthritis**: The ACR/Arthritis Foundation guidelines for the treatment of Juvenile Idiopathic Arthritis (2019) are specific to juvenile non-systemic polyarthritis, sacroiliitis, and enthesitis.[8] For patients without risk factors, initial therapy with a DMARD is conditionally recommended over a biologic (including Actemra). Biologics (e.g., Actemra) are conditionally recommended as initial treatment when combined with a DMARD over biologic monotherapy.
- **Rheumatoid Arthritis**: Guidelines from the American College of Rheumatology (ACR) for the treatment of rheumatoid arthritis (2015) have tumor necrosis factor (TNF) inhibitors and non-TNF biologics (such as Actemra) equally positioned as a recommended therapy following a trial of a conventional synthetic DMARD (e.g., methotrexate, leflunomide, hydroxychloroquine, sulfasalazine).[10]
- **Systemic Juvenile Idiopathic Arthritis**: The 2013 update of the 2011 ACR recommendations for the treatment of SJIA mention Actemra as a second- or third-line agent in patients with active systemic features and varying degrees of synovitis and in patients without active systemic features and varying degrees of synovitis.[9] Nonsteroidal anti-inflammatory drugs NSAIDs, systemic glucocorticoids, Kineret, TNF inhibitors, and MTX are among other treatment options.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Actemra subcutaneous. Because of the specialized skills required for evaluation and diagnosis of a patient treated with Actemra subcutaneous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Actemra subcutaneous to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the approval duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

All reviews for use of Actemra subcutaneous for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Actemra Subcutaneous is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Giant Cell Arteritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following criteria (i and ii):
     - **i.** Patient has tried one systemic corticosteroid; AND
       Note: An example of a systemic corticosteroid is prednisone.
     - **ii.** The medication is prescribed by or in consultation with a rheumatologist.
   - **B)** Patient is Currently Receiving Actemra (Subcutaneous or Intravenous). Approve for 1 year if the patient had a response, as determined by the prescriber.
     Note: Examples of response include reduced corticosteroid dose, normalization of acute phase reactants (e.g., erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]), reduction or resolution of signs or symptoms of GCA. The patient may not have a full response, but there should have been a recent or past response to Actemra subcutaneous or intravenous.

2. **Interstitial Lung Disease Associated with Systemic Sclerosis.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets all of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has elevated acute phase reactants, defined as at least one of the following (a, b, or c):
       - **a)** C-reactive protein (CRP) ≥ 6 mg/mL; OR
       - **b)** Erythrocyte sedimentation rate (ESR) ≥ 28 mm/h; OR
       - **c)** Platelet count ≥ 330 x 10^9/L; AND
     - **iii.** Forced vital capacity (FVC) is > 55% of the predicted value; AND
     - **iv.** Diagnosis is confirmed by high-resolution computed tomography; AND
     - **v.** Medication is prescribed by or in consultation with a pulmonologist or a rheumatologist.
   - **B)** Patient is Currently Receiving Actemra (Subcutaneous or Intravenous). Approve if the patient meets all of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient had adequate efficacy, demonstrated by ≤ 10% decrease in predicated forced vital capacity (FVC) over the past year while on Actemra; AND
     - **iii.** Medication is prescribed by or in consultation with a pulmonologist or a rheumatologist.

3. **Polyarticular Juvenile Idiopathic Arthritis (PJIA).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets BOTH of the following criteria (i and ii):
     - **i.** Patient meets one of the following conditions (a, b, c, or d):
       - **a)** Patient has tried one other systemic therapy for this condition; OR
         Note: Examples of other systemic therapies include methotrexate, sulfasalazine, leflunomide, or a nonsteroidal anti-inflammatory drug (NSAID). A biologic (refer to **Appendix** for examples of biologics used for juvenile idiopathic arthritis) also counts as a trial of one systemic therapy.
       - **b)** Patient will be starting on Actemra subcutaneous concurrently with methotrexate, sulfasalazine, or leflunomide; OR
       - **c)** Patient has an absolute contraindication to methotrexate, sulfasalazine, or leflunomide; OR
         Note: Examples of absolute contraindication to methotrexate include pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, and blood dyscrasias; OR
       - **d)** Patient has aggressive disease, as determined by the prescriber; AND
     - **ii.** The medication is prescribed by or in consultation with a rheumatologist.
   - **B)** Patient is Currently Receiving Actemra (Subcutaneous or Intravenous). Approve for 3 years if the patient had a response, as determined by the prescriber.
     Note: Examples of response include improvement in limitation of motion; less joint pain or tenderness; improved function or activities of daily living; decreased duration of morning stiffness or fatigue; reduced dosage of corticosteroids; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values. The patient may not have a full response, but there should have been a recent or past response to Actemra subcutaneous or intravenous.

4. **Rheumatoid Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets the following (i and ii):
     - **i.** Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND
       Note: Examples of conventional DMARDs include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a

trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic (refer to **Appendix** for examples of biologics used for rheumatoid arthritis). A patient who has already tried a biologic for rheumatoid arthritis is not required to "step back" and try a conventional synthetic DMARD.

ii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Actemra (Subcutaneous or Intravenous). Approve for 3 years if the patient had a response, as determined by the prescriber.

Note: Examples of response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids. The patient may not have a full response, but there should have been a recent or past response to Actemra subcutaneous or intravenous.

5. Systemic Juvenile Idiopathic Arthritis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):

i. Patient has tried one other systemic therapy for this condition; AND

Note: Examples of other systemic therapies include a corticosteroid (oral, intravenous), a conventional synthetic disease-modifying antirheumatic drug (DMARD) [e.g., methotrexate, leflunomide, sulfasalazine], or a 1-month trial of a nonsteroidal anti-inflammatory drug (NSAID). A previous trial of a biologic such as Kineret (anakinra subcutaneous injection), a tumor necrosis factor (TNF) inhibitor (e.g., an etanercept product, an adalimumab product, or an infliximb product, or Ilaris [canakinumab subcutaneous injection]) also counts towards a trial of one other systemic therapy for SJIA.

ii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Actemra (Subcutaneous or Intravenous). Approve for 3 years if the patient had a response, as determined by the prescriber.

Note: Examples of response include improvement in limitation of motion; less joint pain or tenderness; decreased duration of morning stiffness or fatigue; improved function or activities of daily living; reduced dosage of corticosteroids; less joint pain or tenderness; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values. The patient may not have a full response, but there should have been a recent or past response to Actemra subcutaneous or intravenous.

Other Uses with Supportive Evidence

6. Polymyalgia Rheumatica. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets the following criteria (i and ii):

i. Patient has tried one systemic corticosteroid; AND

Note: An example of a systemic corticosteroid is prednisone.

ii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Actemra (Subcutaneous or Intravenous). Approve for 1 year if the patient had a response, as determined by the prescriber.

Note: Examples of response include reduced corticosteroid dose, normalization of acute phase reactants (e.g., erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]), reduction or resolution of signs or symptoms of PMR. The patient may not have a full response, but there should have been a recent or past response to Actemra subcutaneous or intravenous.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Actemra Subcutaneous is not recommended in the following situations:

1. **Concurrent use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (DMARD).** Data are lacking evaluating concomitant use of Actemra SC another biologics or with a targeted synthetic DMARD for an inflammatory condition (see **Appendix** for examples).[1,11] Combination therapy with biologics and/or biologics + targeted synthetic DMARDs has a potential for a higher rate of adverse effects and lack of controlled trial data in support of additive efficacy.[12] Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate (MTX), leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Actemra SC.

2. **COVID-19 (Coronavirus Disease 2019).** Forward all requests to the Medical Director.
   Note: This includes requests for cytokine release syndrome associated with COVID-19.

2. **Crohn's Disease.** In a 12-week pilot study conducted in Japan, 36 adults with active Crohn's disease (Crohn's Disease Activity Index [CDAI] ≥ 150 and increased C-reactive protein [CRP]) were randomized, in a double-blind fashion to IV Actemra 8 mg/kg every 2 weeks; or alternating infusions of Actemra 8 mg/kg every 4 weeks and placebo (i.e., alternating with placebo every 2 weeks), or to placebo every 2 weeks.[13] At baseline the CDAI means ranged from 287 to 306. Patients had been treated with corticosteroids, mesalamine-type drugs, metronidazole, or elemental diet. Six patients in the placebo group, 4 on Actemra every 4 weeks and 1 on Actemra every 2 weeks dropped out. The mean reduction in the CDAI score in the Actemra 8 mg/kg every 2 week group was 88 points – from mean 306 to 218. Further studies are needed.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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