MEDICAL MUTUAL®

Drug Policy

Policy:	**201835**	**Initial Effective Date: 02/18/2016**
Code(s):	**HCPCS J3262**	**Annual Review Date: 11/15/2018**
SUBJECT:	**Actemra SC ® (tocilizumab)**	**Last Revised Date: 11/15/2018**

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

Actemra for subcutaneous (SC) injection is a recombinant humanized interleukin-6 (IL-6) receptor inhibitor. IL-6 is a pro-inflammatory cytokine that is involved in various physiologic processes. Actemra SC has demonstrated efficacy and is indicated for the treatment of rheumatoid arthritis (RA) in adults with moderate to severe active RA who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Actemra SC has been shown to inhibit and slow structural joint damage, improve physical function, and achieve a major clinical response in patients taking methotrexate (MTX). In addition to RA, Actemra SC is also indicated in adults with giant cell arteritis (GCA) and polyarticular juvenile idiopathic arthritis (PJIA).. It is recommended to be given once weekly and may be given in combination with a tapering course of glucocorticoids. Actemra SC can be used alone following the discontinuation of glucocorticoids.

POLICY STATEMENT

This policy involves the use of Actemra SC. Prior authorization is recommended for medical benefit coverage of Actemra SC. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Actemra SC as well as the monitoring required for AEs and long-term efficacy, initial approval requires Actemra SC be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

The Site of Care Medical Necessity Criteria applies to initial therapy and reauthorizations under the medical benefit.

RECOMMENDED AUTHORIZATION CRITERIA

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

Food and Drug Administration (FDA)-Approved Indications

1. **Giant Cell Arteritis (GCA).**
   - **A) Initial Therapy.** Approve for 6 months if the patient meets the following criteria (i, ii and iii):
     - **i.** The patient has tried one systemic corticosteroid (e.g., prednisone); AND
     - **ii.** Actemra SC is prescribed by or in consultation with a rheumatologist; AND
     - **iii.** Site of care medical necessity is met*
   - **B) Patient is Currently Receiving Actemra (IV or SC).** Approve for 1 year if the patient has had a response (e.g., 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), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Actemra (SC or IV) and site of care medical necessity is met*.

Dosing in GCA. *Dosing must meet the following:* SubQ: 162 mg once every week (in combination with a tapering course of glucocorticoids); based on clinical considerations, may consider 162 mg once every other week (with a tapering course of glucocorticoids). Tocilizumab may be administered as monotherapy following discontinuation of glucocorticoids.

Initial Approval/ Extended Approval.
A) *Initial Approval:6 months*
B) *Extended Approval: 1 year*

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2. 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, ii and iii):
  - **i.** The patient meets one of the following conditions (a, b, c, or d):
    - **a)** The patient has tried one other agent for this condition (e.g., methotrexate [MTX], sulfasalazine, leflunomide, or a nonsteroidal anti-inflammatory drug [NSAID]).
      NOTE: A biologic (e.g., an etanercept product [Enbrel, Erelzi], an adalimumab product [Humira], Orencia [abatacept IV infusion, abatacept SC injection], an infliximab product [Remicade, Inflectra, Renflexis], or Kineret [anakinra SC injection]) also counts as a trial of one agent for JIA; OR
    - **b)** The patient will be starting on Actemra SC concurrently with methotrexate (MTX), sulfasalazine, or leflunomide; OR
    - **c)** The patient has an absolute contraindication to methotrexate (MTX) [e.g., pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, blood dyscrasias], sulfasalazine, or leflunomide; OR
    - **d)** The patient has aggressive disease, as determined by the prescribing physician; AND
  - **ii.** Actemra SC is prescribed by or in consultation with a rheumatologist; AND
  - **iii.** Site of care medical necessity is met*

B) Patients Currently Receiving Actemra (IV or SC). Approve for 1 year if the patient has had a response (e.g., has 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), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Actemra IV or SC. And site of care medical necessity is met*.

Dosing in PJIA. *Dosing must meet the following:* SubQ:
<30 kg: 162 mg once every 3 weeks
≥30 kg: 162 mg once every 2 weeks

Initial Approval/ Extended Approval.
A) *Initial Approval:4 months*
B) *Extended Approval: 1 year*

3. Rheumatoid Arthritis (RA).

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

- **i.** The patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months (e.g., methotrexate [oral or injectable], leflunomide, hydroxychloroquine, and sulfasalazine).
  (NOTE: 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 disease-modifying antirheumatic drug (DMARD) [e.g., Cimzia, Enbrel, Humira, Remicade, Simponi {Aria or SC}, Kineret, Orencia {IV or SC}, and Rituxan]. These patients who have already tried a biologic for RA are not required to "step back" and try a conventional synthetic DMARD); AND
- **ii.** Actemra SC is prescribed by or in consultation with a rheumatologist; AND
- **iii.** The patient is 16 years of age or older; AND
- **iv.** The patient has moderate to severe rheumatoid arthritis; AND
- **v.** Site of care medical necessity is met.*

B) Patients Currently Receiving Actemra (SC or IV). Approve for 1 year if the patient has had a response (e.g., 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), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Actemra (SC or IV). And site of care medical necessity is met*.

Dosing in RA. *Dosing must meet the following:*
SubQ:
<100 kg: 162 mg once every other week; increase to 162 mg once every week based on clinical response
≥100 kg: 162 mg once every week

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Initial Approval/ Extended Approval.
A) *Initial Approval:3 months*
B) *Extended Approval: 1 year*

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Actemra SC has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent use with a Biologic Disease-Modifying Antirheumatic (DMARD) or Targeted Synthetic DMARD.** Actemra should not be administered in combination with another biologic agent for an inflammatory condition (e.g., Cimzia, Enbrel, Humira, Kineret, Orencia, Remicade, Rituxan, or Simponi [Aria or SC]). Combination therapy with two biologic agents is not recommended due to a higher rate of adverse effects with combinations and lack of additive efficacy. Xeljanz should not be used in combination with biologic DMARDs such as Actemra SC. Targeted synthetic DMARDs (e.g., Xeljanz, Otezla® [apremilast tablets]) do not have data supporting use in combination with biologic DMARDs. Due to similar safety concerns (i.e., increased risk of AEs) plus no evidence of additive efficacy, targeted synthetic DMARDs should not be used in combination with biologic DMARDs such as Actemra SC. Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Actemra SC.

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. 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.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a

pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Actemra® [prescribing information]. South San Francisco, CA: Genentech; October 2018.
2. Burmester GR, Rubbert-Roth A, Cantagrel A, et al. A randomised, double-blind, parallel-group study of the safety and efficacy of subcutaneous tocilizumab versus intravenous tocilizumab in combination with traditional disease-modifying antirheumatic drugs in patients with moderate to severe rheumatoid arthritis (SUMMACTA study). *Ann Rheum Dis.* 2014;73(1):69-74.
3. 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.
4. Furst DE, Keystone EC, So AK, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012. *Ann Rheum Dis*. 2013;72 Suppl 2:ii2-34.
5. Xeljanz® tablets [prescribing information]. New York, NY: Pfizer Inc; February 2016.
6. Ito H, Takazoe M, Fukuda Y, et al. A pilot randomized trial of a human anti-interleukin-6 receptor monoclonal antibody in active Crohn's disease. *Gastroenterology*. 2004;126:989-996.
7. Roberts J, Clifford A. Update on the management of giant cell arteritis. *Ther Adv Chronic Dis*. 2017;8(4-5):69-79.
8. Giant cell arteritis. Mayo Foundation for Medical Education and Research Web site. October 2, 2015. Available at: http://www.mayoclinic.org/diseases-conditions/giant-cell-arteritis/basics/definition/con-20023109. Accessed on May 17, 2018.
9. National Institutes of Health, US Department of Health and Human Services. National Institute of Arthritis and Musculoskeletal and Skin Diseases Web site. Available at: https://www.catalog.niams.nih.gov/index.cfm. Search terms: Polymyalgia rheumatic and giant cell arteritis. Accessed on May 17, 2018.
10. Tuckwell K, Collinson N, Dimonaco S, et al. Newly diagnosed vs. relapsing giant cell arteritis: baseline data from the GiACTA trial. *Semin Arthritis Rheum*. 2017;46(5):657-664.
11. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of tocilizumab in giant-cell arteritis. *N Engl J Med*. 2017 ;377(4):317-328.
12. Smolen JS, Aletaha D, Bijlsma JW, et al; T2T Expert Committee. Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis*. 2010;69:631-637.
13. Singh JA, Cameron DR. Summary of AHRQ's comparative effectiveness review of drug therapy for rheumatoid arthritis (RA) in adults--an update. *J Manag Care Pharm*. 2012;18(4 Supp C):S1-18.
14. Dejaco C, Ramiro S, Duftner C, et al. Recommendations for the use of imaging in large vessel vasculitis in clinical practice. *Ann Rheum Dis*. 2018;77(5):636-643.
15. Lally L, Forbess L, Hatzis C, Spiera R. Brief report: a prospective open-label Phase IIa trial of tocilizumab in the treatment of polymyalgia rheumatica. *Arthritis Rheumatol*. 2016;68(10):2550-2554.
16. Devauchelle-Pensec V, Berthelot JM, Cornec D, et al. Efficacy of first-line tocilizumab therapy in early polymyalgia rheumatica: a prospective longitudinal study. *Ann Rheum Dis*. 2016;75(8):1506-1510.
17. Macchioni P, Boiardi L, Catanoso M, et al. Tocilizumab for polymyalgia rheumatica: report of two cases and review of the literature. *Semin Arthritis Rheum*. 2013;43(1):113-118.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

*MMO Site of Care Medical Necessity Criteria:

- Medications in this policy will be administered in a non-hospital facility based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless *at least one* of the following are met†:

    1. Age less than18 years*; or
    2. Clinically unstable based upon documented medical history (e.g., patient is hemodynamically unstable); or
    3. History of a severe adverse event from previous administration of the prescribed medication; or
    4. Requested medication is being administered as follows:
        - part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer; or
        - administered with dialysis; or
    5. Physical or cognitive impairment and caregiver is not available to assist with safe administration of prescribed medication in the home; or
    6. No doses will be allowed in a hospital facility based location; or
    7. Experiencing adverse events that are not managed by premedication or resources available at a non-hospital facility based location.

* Effective 01/01/2019, age criterion applies to 18 years of older. Age at original effective date (03/01/2016) was 21 years or older.
†This criterion does not apply to Medicare or Medicare Advantage members.

Prior approval is required for HCPCS Codes J3262

HCPCS Code(s):	
J3262	Injection, tocilizumab, 1 mg