Effective Date: 04/2014
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Policy Number: C10265-A

Actemra (tocilizumab)

PRODUCTS AFFECTED

Actemra (tocilizumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Moderately to severely active rheumatoid arthritis (RA), Polyarticular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, temporal arteritis, also known as giant cell arteritis (GCA), chimeric antigen receptor (CAR) T-cell-induced severe or life- threatening cytokine release syndrome (CRS), systemic sclerosis-associated interstitial lung disease (SSc-ILD)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

Drug and Biologic Coverage Criteria

FOR ALL INDICATIONS:

1. (a) Prescriber attests member has had a negative TB screening or TB test result within the last 12 months for initial and continuation of therapyrequests
   OR
   (b) For members who have a positive test for latent TB, provider documents member has completed a treatment course (a negative chest x-ray is also required every 12 months) OR that member has been cleared by an infectious disease specialist to begin treatment
   AND
2. Member is not on concurrent treatment or will be used in combination with other TNF- inhibitor, biologic response modifier or other biologic DMARDs, Janus kinase Inhibitors, or Phosphodiesterase 4 inhibitor (i.e., apremilast, tofacitinib, baricitinib) as verified by prescriber attestation, member medication fill history, or submitted documentation
   AND
3. Prescriber attests member does not have an active infection, including clinically important localized infections
   AND
4. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes,please submit documentation including medication(s) tried, dates of trial(s) and reason for treatmentfailure(s)

A. MODERATE TO SEVERE RHEUMATOID ARTHRITIS:

1. Documentation of moderate to severe rheumatoid arthritis diagnosis
   AND
2. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal
   AND
3. (a) Member is concurrently receiving methotrexate
   OR
   (b) Member tried, failed, or has an FDA labeled contraindication or intolerance to methotrexate, asdetermined by the prescribing physician AND member has tried one additional disease-modifying antirheumatic drug (DMARD) (brand or generic; oral or injectable) for at least 3 months *(NOTE: An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the Member has already had a 3-month trial of at least one biologic. These patients who have already tried a biologic for RA are not required to "step back" and try a conventional synthetic DMARD)*
   OR
   (c) Member has early RA (defined as disease duration of < 6 months) with at least one of the following features of poor prognosis: functional limitation (e.g., based on Health Assessment Questionnaire Disability Index [HAQ-DI] score); extra articular disease such as rheumatoid nodules, RA vasculitis, or Felty's syndrome; positive rheumatoidfactor or anti- cyclic citrullinated protein (anti-CCP) antibodies; or bony erosions by radiograph

B. JUVENILE IDIOPATHIC ARTHRITIS (SYSTEMIC AND POLYARTICULAR):

1. Member must have a diagnosis of systemic juvenile idiopathic arthritis (SJIA) or polyarticular juvenile idiopathic arthritis (PJIA) in children 2 years of age or older
   AND
2. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal
   AND
3. (a) FOR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: Documentation of serious side effect, clinical contraindication, or treatment failure to an adequate trial(up to 12 weeks) of TWO of the following: NSAIDs, glucocorticoids, methotrexate, leflunomide, anakinra (Kineret), or canakinumab (Ilaris)

OR
(b) FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS: Documentation of serious side effect, clinical contraindication, or treatment failure to an adequate trial (generally ≥12 weeks) of
≥1 of the following: Methotrexate, hydroxychloroquine, sulfasalazine, azathioprine, leflunomide

C. GIANT CELL ARTERITIS (GCA):
1. Member must have confirmed diagnosis of giant cell arteritis by results of a temporal-artery biopsy showing features of giant-cell arteritis or on evidence of large- vessel vasculitis on angiography, computed tomographic or magnetic resonance angiography, or positron-emission tomography OR high clinical suspicion despite negativebiopsy and imaging
AND
2. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal
AND
3. Documented disease activity defined as unequivocal evidence of cranial symptoms of giant-cell arteritis or polymyalgia rheumatica and increased concentrations of serum acute-phase reactants (ESR > 30 mm/hour or CRP > 1 mg/dL)
AND
4. Member must have documented need for a glucocorticoid sparing agent use such as: presence of significant premorbid diseases, emergence of significant glucocorticoid-related side effects during the course of treatment, a relapsing course necessitating protracted glucocorticoid use, preexisting diabetes mellitus on treatment, osteoporosis, or significant obesity
AND
5. (a) Documentation of an inadequate clinical response to a compliant regimen of methotrexate or ≥3 months
OR
(b) Contraindication to methotrexate, as evidenced by ≥1 of the following: Known hypersensitivity to methotrexate, History of intolerance or adverse event to methotrexate, currently pregnant or planning for pregnancy, Breastfeeding, Alcoholism, Alcoholic liver disease or other chronic liver disease, Elevated liver transaminases, Interstitial pneumonitis or clinically significant pulmonary fibrosis, Renal impairment (CrCl <40mL/min), Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia), Myelodysplasia, Significant drug interaction, Overt or laboratory evidence of immunodeficiency, Active pulmonary disease, Peptic ulcer disease

CI. CYTOKINE RELEASE SYNDROME (CAR-T THERAPY INDUCED): APPROVED ONLY IF CART- T IS APPROVED BY TRANSPLANT TEAM. VERIFICATION OF CAR-T IS REQUIRED DOCUMENTATION

CII. SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSc-ILD) (subcutaneous syringes only):
1. Documented diagnosis of systemic sclerosis-associated interstitial lung disease
AND
2. Documentation of chest high resolution computed tomography (HRCT) scan confirming diagnosis of interstitial lung disease [DOCUMENTATION REQUIRED]
AND
3. Documentation member has elevated acute-phase reactants as documented by at least one of the following: CRP level > 6mg/liter, erythrocyte sedimentation rate > 28 mm/hour, platelet count greater than 330 x 10^9/liter [DOCUMENTATIONREQUIRED]
AND
4. Tocilizumab is not being prescribed for use with nintedanib (Ofev)
AND

5. Prescriber attests that member has tried and failed or has a labeled contraindication to mycophenolate mofetil.

CONTINUATION OF THERAPY:

A. ALL INDICATIONS (EXCEPTCRS):

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation (documentation Required)
   AND
2. Documentation of no intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms.
   AND
4. (a) Prescriber attests member has had a negative TB screening or TB test result within the last 12 months for initial and continuation of therapyrequests
   OR
   (b) For members who have a positive test for latent TB, provider documents member has completed a treatment course (a negative chest x-ray is also required every 12 months) OR that member has been cleared by an infectious disease specialist to begin treatment

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of therapy: 12 months.

PRESCRIBER REQUIREMENTS:

CYTOKINE RELEASE SYNDROME (CAR-T THERAPY INDUCED): Prescribed by or in consultation with a board-certified oncologist.
SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSc-ILD): Prescribed by or in consultation with a board-certified rheumatologist or pulmonologist.
ALL OTHER INDICATIONS: Prescribed by or in consultation with a board-certified rheumatologist [If prescribed in consultation, consultation notes must be submitted within initial request and reauthorization requests]

AGE RESTRICTIONS:

PJIA, SJIA and CAR T-cell-induced cytokine release syndrome: at least 2 years of age and older.
All other indications: 18 years of age and older

QUANTITY:

CYTOKINE RELEASE SYNDROME (CAR-T THERAPY INDUCED): max 8 single dose vials per lifetime.
NOTE: PLEASE SEND TO MEDICAL DIRECTOR FOR REVIEW AND AUTHORIZATION CONCURRENTLY W ITH CART THERAPY

ALL OTHER INDICATIONS:
Subcutaneous:
Rheumatoid arthritis: Up to 162 mg every week
Giant cell arteritis: Up to 162 mg every week
SSc- ILD: 162 mg every week
PJIA: < 30 kg – 162 mg every 3 weeks; 30 kg or greater – 162 mg every 2 weeks SJIA: <30 kg – 162 mg every 2 weeks; 30 kg or greater – 162 mg every week

Intravenous:
Rheumatoid arthritis: 4 mg/kg every 4 weeks, may increase to 8 mg/kg every 4 weeks, not to exceed 800 mg per infusion
PJIA: < 30 kg – 10 mg/kg every 4 weeks; 30 kg or greater – 8 mg/kg every 4 weeks SJIA: < 30 kg – 12 mg/kg every 4 weeks; 30 kg or greater – 8 mg/kg every 2 weeks
CRS: < 30 kg – 12 mg/kg; 30 kg or greater – 8 mg/kg every 4 weeks, not to exceed 800 mg per infusion

Maximum Quantity Limits –
SC: 4 packages (4 syringes) per 28 days
IV: 80 mg/4 mL vial: 1 vial per 14 days, 200 mg/10 mL vial: 1 vial per 14 days, 400 mg/20 mL vial: 2 vials per 14 days

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that is a non-hospital facility-based location.
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.
Note: Site of Care Utilization Management Policy applies for Actemra (tocilizumab) IV. For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous, Subcutaneous

DRUG CLASS:
Interleukin-6 Receptor Inhibitors

FDA-APPROVED USES:
Actemra IV and SQ: Indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs). Indicated for the treatment of active polyarticular juvenile idiopathic arthritis and active systemic juvenile idiopathic arthritis in patients 2 years of age and older.

Actemra SQ (only): Indicated for the treatment of giant cell arteritis (GCA) in adult patients. Indicated for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease.

Actemra IV (only): chimeric antigen receptor (CAR) T-cell-induced severe or life-threatening cytokine release syndrome (CRS)' in adults and pediatric patients 2 years of age and older.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
OBJECTIVE MEASURES FOR RA:

[Clinical Disease Activity Index (CDAI), Disease Activity Score with 28-joint counts

(erythrocyte sedimentation rate or C-reactive protein), Member Activity Scale (PAS or PAS- II),Routine Assessment of Member Index Data with 3 measures, Simplified Disease Activity Index (SDAI)] OBJECTIVE MEASURES FOR PJIA:
Global Arthritis Score (GAS), Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS), Disease Activity Score based on 28-joint evaluation (DAS28), Simple Disease Activity Index (SDAI), Health Assessment Questionnaire disability index (HAQ-DI), Visual Analogue Scale (VAS), Likert scales of global response or pain by the member or global response by the physician, Joint tenderness and/or swelling counts, Laboratory data

Table 1. The American College of Rheumatology/European League Against Rheumatism criteria for the classification of systemic sclerosis (SSc)*

Item	Sub-item(s)	Weight/score
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints *(sufficient criterion)*		9
Skin thickening of the fingers *(only count the higher score)*	Puffy fingers Sclerodactyly of the fingers (distal to the metacardpophalangeal joints but proximal to the proximal interphalangeal joints)	2 4
Fingertip lesions *(only count the higher score)*	Digital tips ulcers Fingertip pitting scars	2 3
Telangiectasia	-	2
Abnormal naifold capillaries	-	2
Pullmonary arterial hypertension and/or interstitial lung disease *(maximum score is 2)*	Pulmonary arterial hypertension Interstitial lung disease	2 2
Raynaud's phenomenon	-	3
SSc-related autoantibodies (anticentromere, anti-topoisomerase 1 [anti-Scl-70], anti-RNA polymerase III) (maximum score is 3)	Anticentromere Anti-topoisomerase I Anti-RNA polymerase III	3

*These criteria are applicable to any patient considered for inclusion in an SSc study. The criteria not applicable to patients with skin thickening sparing the fingers or to patients who have a scleroderma-like disorder that better explains their manifestations (e.g., nephrogenic sclerosing fibrosis, generalized morphea, eosinophilic fasciitis, scleroderma diabeticorum, scleromyxedema, erythromelalgia, porphyria, lichen sclerosis, graft-versus-host disease, diabetic cheiroarthropathy).
+The total score is determined by adding the maximum weight (score) in each category. Patients with a total score of ≥9 are classified as having definitive SSc.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Tocilizumab (Actemra) is a recombinant humanized anti-human interleukin-6 (IL-6) receptor monoclonal antibody (IgG1κ). The drug binds to membrane-bound (mIL-6R) and soluble (sIL- 6R) forms of the interleukin-6 receptor, thereby reducing the inflammatory process by inhibiting signaling through these receptors. Interleukin-6 is a pleiotropic pro-inflammatory cytokine involved in multiple phases of the inflammatory response, including T-cell activation and induction of immunoglobulin secretion. 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 patientstaking methotrexate (MTX). In addition to RA, Actemra SC is also indicated in adults with giant cell arteritis (GCA). 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. The

subcutaneous formulation is also indicated for SSc-ILD and has been shown slow the rate of decline in pulmonary function in adult patients. Actemra is also available as an intravenous (IV) formulation which, in addition to RA, is indicated in patients 2 years of age and older for the treatment of active systemic juvenile idiopathic arthritis (SJIA) or polyarticular juvenile idiopathic arthritis (PJIA). The IV formulation is not indicated in GCA or SSc-ILD.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Actemra (tocilizumab) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy.

OTHER SPECIAL CONSIDERATIONS:
All other uses of Actemra (tocilizumab) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J3262	Injection, tocilizumab, 1 mg

AVAILABLE DOSAGE FORMS:
Actemra 80MG/4ML
Actemra 200MG/10ML
Actemra 400MG/20ML
Actemra Pen 162MG/0.9ML
Actemra162MG/0.9ML

REFERENCES

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4. Smolen JS, Beaulieu A, Rubbert-Roth A, et al. for the OPTION Investigators. Effectofinterleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (OPTION study): a double-blind, placebo-controlled, randomized trial. Lancet. 2008;371:987-97.
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treatment outcomes in patients with rheumatoid arthritis refractory to anti-tumor necrosis factor biologicals: results from a 24-hour week multicenter randomized placebo-controlled trial. Ann Rheum Dis. 2008;67:1516-1523.
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