CRITERIA EFFECTIVE DATES:

<table>
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<tr>
<th>ORIGINAL EFFECTIVE DATE</th>
<th>LAST REVIEWED DATE</th>
<th>NEXT REVIEW DATE</th>
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<tr>
<td>04/2014</td>
<td>8/26/2020</td>
<td>8/26/2021</td>
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J CODE | TYPE OF CRITERIA | LAST P&T APPROVAL/VERSION
---|------------------|-----------------------------
J3262 Injection, tocilizumab, 1 mg | RxPA | Q4 2020 20201028C10265-A

PRODUCTS AFFECTED:
Actemra (tocilizumab)

DRUG CLASS:
Interleukin-6 Receptor Inhibitors

ROUTE OF ADMINISTRATION:
Intravenous, Subcutaneous

PLACE OF SERVICE:
Specialty Pharmacy or Buy and Bill
The recommendation is that medications in this policy will be for pharmacy benefit coverage and the IV infusion products administered in a place of service that is a non-hospital facility based location (i.e., home infusion provider, provider’s office, free-standing ambulatory infusion center) and the Pre-Filled Syringe product for self-administered.

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

FDA-APPROVED USES:
Actemra IV and SQ: Moderately to severely active rheumatoid arthritis (RA), active polyarticular or systemic juvenile idiopathic arthritis (>2 years)

Actemra SQ (only): temporal arteritis, also known as giant cell arteritis (GCA)

Actemra IV (only): chimeric antigen receptor (CAR) T-cell-induced severe or life- threatening cytokine release syndrome (CRS)

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Moderately to severely active rheumatoid arthritis (RA), Polyarticular juvenile idiopathic arthritis, active 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)
REQUIRED MEDICAL INFORMATION:
FOR ALL INDICATIONS:

1. (a) Negative TB test within the last 12 months for initial and continuation of therapy requests
   OR
   (b) If member tests positive for latent TB, there must be documentation showing member completed a treatment course for TB OR that member has been cleared by an infectious disease specialist to begin treatment with INFLIXIMAB
   OR
   (c) For members who have tested positive for latent TB and have been treated, a negative chest x-ray is required every 12 months
   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)
   AND
3. Member does not have an active infection, including clinically important localized infections
   AND
4. IF THIS IS A NON-FORMULARY 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 treatment failure(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, as determined 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 rheumatoid factor or anti-cyclic citrullinated protein (anti-CCP) antibodies; or bony erosions by radiograph

B. JUVENILE IDIOPATHIC ARTHRITIS (ACTIVE SYSTEMIC AND ACTIVEPOLYARTICULAR):
   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. Documentation of drug failure or serious side effects to an adequate trial (12 weeks) of TWO of the following: glucocorticoids, methotrexate or 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 negative biopsy and imaging AND

2. 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

3. 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

4. (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

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

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months.

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 WITH CART THERAPY

ALL OTHER INDICATIONS: 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

When requests for off-label dosing, dose escalation, or dose intensification are received, requests will be reviewed for evidence that current or standard dosing is not adequate to produce a therapeutic level of drug (e.g., pharmacokinetic failure), clinical failure or significant loss of response is present, and the requested dosing is established as safe and effective for the condition. There are certain situations where no additional amount of drug is likely to produce or recapture clinical effect because the condition is no longer responsive to the drug (e.g., pharmacodynamic failure) or the drug cannot reach the site of activity at sufficient levels.

The following items will assist reviewers in determining if the requested dosing is medically necessary:

- FDA or compendium-supported dosing and therapeutic monitoring recommendations for the drug
- Member claims/adherence history
- Clinical documentation of the member’s response to current or standard dosing regimens
Prior Authorization Criteria

(disease activity indices if commonly used in clinical practice or documentation to approximate them may be necessary to demonstrate the response)

• In conjunction with documented clinical failure or loss of response or wearing off of effect, test results that demonstrate failure of current or standard dosing to reach established treatment thresholds (e.g., established therapeutic monitoring recommendations)

• If applicable, documentation showing the member does not have conditions which make achieving a therapeutic level of drug unlikely even with dose intensification (e.g., dose intensification may be futile due to the presence of anti-drug antibodies, protein losing enteropathy, nephrotic syndrome, severe drug excretion or malabsorption issues, etc.)

• In certain situations, documentation or peer-to-peer determination that re-induction cannot be tried to recapture response as an alternative to long term dose escalation or intensification

PRESCRIBER REQUIREMENTS:

CYTOKINE RELEASE SYNDROME (CAR-T THERAPY INDUCED): Prescribed by or in consultation with an oncologist.

ALL OTHER INDICATIONS: Prescribed by or in consultation with a rheumatologist

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

CONTINUATION OF THERAPY:

A. ALL INDICATIONS (EXCEPT CRS):
   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) Negative TB test within the last 12 months for initial and continuation of therapy requests
      OR
      (b) If member tests positive for latent TB, there must be documentation showing member completed a treatment course for TB OR that member has been cleared by an infectious disease specialist to begin treatment
      OR
      (c) For members who have tested positive for latent TB and have been treated, a negative chest x-ray is required every 12 months

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Acetmra (tocilizumab) are considered experimental/investigational and therefore, will follow Molina’s Off-Label policy.

OTHER SPECIAL CONSIDERATIONS:

All other uses of Acetmra (tocilizumab) are considered experimental/investigational and therefore, will follow Molina’s Off-Label policy.
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 patients taking 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. 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.

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

Molina Healthcare, Inc. covers injectable/infused treatment in a hospital outpatient setting or at a hospital-affiliated infusion suite* when the level of care is determined to be medically necessary. Considerations used to determine if an alternative level of care is not suitable may include the following findings:

1. The patient is clinically unstable based on documented medical history and susceptible to complication with drug administration (e.g., cardiopulmonary or renal dysfunction, risk for fluid overload)
2. The requested medication is administered as part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer or with dialysis
3. The patient exhibits physical or cognitive impairment and a capable caregiver is not available to assist with safe administration of prescribed medication in the home
4. It is the patient’s first dose of the medication or it is being re-initiated after at least 12 months*
5. The patient has experienced adverse events with past administration of the drug and cannot be managed by premedication or resources available at a non-hospital facility-based location (NHFBL)
6. Documented history of difficulty establishing and maintaining patent vascular access, or is not a candidate for a mode of long-term vascular access during the duration of treatment.
prescribed treatment

Note: a hospital outpatient setting, or a hospital-affiliated infusion suite is expected to have immediate access to specific services of a medical center/hospital setting, including having emergency resuscitation equipment and personnel (ACLS protocol), emergency services, and inpatient admission or intensive care, if necessary

REFERENCES: