I. Medication Description

Actemra (tocilizumab) is an interleukin-6 (IL-6) receptor inhibitor indicated for the treatment of rheumatoid arthritis in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies. Tocilizumab binds specifically to both soluble and membrane bound IL-6 receptors and has been shown to inhibit IL-6 mediated signaling through these receptors. IL-6 has been shown to be involved in many physiological processes such as T-cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis, and stimulation of hematopoietic precursor cell proliferation and differentiation. IL-6 is produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis.

II. Position Statement

Coverage is determined through a prior authorization with supporting clinical documentation for every request.

III. Policy

Medical Benefit: See Sections A, C, D, and E
Formulary 1: See Section B, C, D and E
Formulary 2: See Section B, C, D and E
Formulary 3/Exclusive: See Section B, C, D and E
Formulary 4/AON: See Section B, C, D and E

A. Coverage of IV Actemra is provided for chimeric antigen receptor (CAR) T-cell induced Cytokine Release Syndrome (CRS) when the following criteria have been met:
   - Prescribed by a hematologist/oncologist AND
   - Criteria for concurrent CAR T-cell therapy have been met (please see pertinent CAR T-cell therapy policy for medication-specific coverage criteria) AND
   - The requested use is supported by FDA-approved prescribing information and/or the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (NCCN Guidelines®) and/or NCCN Drugs & Biologics Compendium (NCCN Compendium®) with a recommendation of category level 1 or 2A.

B. Coverage of SC Actemra is provided for the treatment of Giant Cell Arteritis (GCA) when the following criteria have been met:
   - Prescribed by a rheumatologist AND
   - Member is 18 years of age or older AND
• Medication is used in combination with a tapering or ongoing glucocorticoid therapy (unless contraindicated) OR
• Medication is used as monotherapy following discontinuation of glucocorticoids.

C. Coverage of Actemra is provided for Juvenile Idiopathic Arthritis (JIA) when the following criteria are met:
   • For IV Actemra (medical benefit) for the treatment of Polyarticular or Systemic JIA:
     ▪ Prescribed by a rheumatologist AND
     ▪ Member is 2 years of age or older AND
     ▪ Member has had a previous inadequate response to or has been intolerant of at least one disease-modifying anti-rheumatic drug (DMARD).
   • For SC Actemra (prescription benefit) for the treatment of JIA:
     ▪ Prescribed by a rheumatologist AND
     ▪ Member is 2 years of age or older AND
     ▪ Member has had a previous inadequate response to or has been intolerant of at least one disease-modifying anti-rheumatic drug (DMARD) AND
     ▪ For the treatment of Polyarticular JIA (PJIA) only:
       • Member has tried the plan-preferred medication, Humira.

D. Coverage of Actemra is provided for Rheumatoid Arthritis when the following are met:
   • Prescribed by a rheumatologist AND
   • Member is 18 years of age or older AND
   • Member has moderate to severe active disease AND
   • Member has had a previous inadequate response to or has been intolerant of at least one disease-modifying anti-rheumatic drug (DMARD) AND
   • For medical benefit claims only: Patient has tried therapy with at least one of the following plan-preferred medications (Remicade or Simponi Aria), unless there is a documented contraindication to the use of both agents.

E. Step therapy criteria outlined in C and D apply unless the following criteria are met:
   • When requesting coverage of a brand medication for which a plan-preferred A/B rated generic is available, coverage will be provided when there is sufficient evidence that the use of the A/B rated generic equivalent has resulted in inadequate results AND
   • At least one of the following is met:
     o The plan-preferred medications are contraindicated or will likely cause an adverse reaction by or physical or mental harm to the member.
     o The plan-preferred medications are expected to be ineffective based on the known clinical history and conditions of the member and the member’s prescription drug regimen.
     o The member has tried the plan-preferred medications or another prescription drug in the same pharmacologic class or with the same mechanism of action and such prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event.
     o The member is stable on the medication selected by their healthcare professional for the medical condition under consideration (where “stable” is defined as receiving the medication for an adequate period of time, have achieved optimal response, and continued favorable outcomes are expected UNLESS the medication was initially selected due to the
availability of a drug sample or a coupon card and the member does not otherwise meet the definition of “stable”).
  
  o The plan-preferred medication is not in the best interest of the member because it will likely cause a significant barrier to the member’s adherence or to compliance with the member’s plan of care, will likely worsen a comorbid condition of the member, or will likely decrease the member’s ability to achieve or maintain reasonable functional ability in performing daily activities.

IV. Quantity Limitations

- **Cytokine Release Syndrome (CRS):**
  - A maximum of 4 IV doses will be approved per treatment
  - For members weighing 30 kg or more: 8 mg/kg, not to exceed 800 mg per dose
  - For members weighing less than 30 kg: 12 mg/kg, not to exceed 800 mg per dose

- **Giant Cell Arteritis:**
  - SC: Up to four 162 mg prefilled syringes every 4 weeks

- **Polyarticular Juvenile Idiopathic Arthritis:**
  - Maximum depends on weight
  - IV:
    - If member is at or above 30kg, max is 8mg/kg every 4 weeks
    - If member is below 30kg, max is 10mg/kg every 4 weeks
  - SC:
    - If member is at or above 30kg, max is 162mg every 2 weeks
    - If member is below 30kg, max is 162mg every 3 weeks

- **Systemic Juvenile Idiopathic Arthritis:**
  - Maximum depends on weight
  - IV:
    - If member is at or above 30kg, max is 8mg/kg every 2 weeks
    - If member is below 30kg, max is 12mg/kg every 2 weeks
  - SC:
    - If member is at or above 30kg, max is 162mg every week
    - If member is below 30kg, max is 162mg every 2 weeks

- **RA:**
  - IV: Maximum of 800mg every 4 weeks
  - SC: Up to four 162 mg prefilled syringes every 4 weeks

V. Coverage Duration

Coverage of Actemra is available as follows:

- **Cytokine Release Syndrome** – 4 doses to be used within a 3 month period and may not be renewed
- **Giant Cell Arteritis** – coverage is provided for 6 months and may be renewed
- **For all other indications** – coverage is provided for 12 months and may be renewed.

VI. Coverage Renewal Criteria
• Cytokine Release Syndrome – coverage may not be renewed
• Giant Cell Arteritis – coverage can be renewed in up to 6 month intervals based upon the following criteria:
  o Clinical response and remission of disease is maintained with continued use AND
  o Absence of unacceptable toxicity from the drug
• For all other indications – coverage can be renewed in up to 12 month intervals based upon the following criteria:
  o Clinical response and remission of disease is maintained with continued use AND
  o Absence of unacceptable toxicity from the drug

VII. Billing/Coding Information

• J3262 – 1 billable unit is 1mg
• Available as:
  o 200mg/10ml (10ml vial) – medical benefit
  o 400mg/20ml (20ml vial) – medical benefit
  o 80mg/4ml (4ml vial) – medical benefit
  o 162mg per 0.9ml prefilled syringe- pharmacy benefit
• Pertinent diagnoses:
  o Cytokine Release Syndrome: No diagnosis code found
  o Giant Cell Arteritis: M31.5, M31.6
  o Rheumatoid arthritis: M05.00, M05.30, M05.60-M05.69, M05.70-M05.79, M06.00-M06.09, M06.1, M06.9
  o Juvenile rheumatoid arthritis: M08.00, M08.20-M08.29, M08.3, M08.40

VIII. Summary of Policy Changes

• 6/1/11: Addition of laboratory marker requirements for coverage of Actemra
• 4/2011: Addition of systemic juvenile idiopathic arthritis indication per new FDA approval
• 1/1/12: Dosage information added with regards to ANC, plts, and AST/ALT; Lab values required for renewal are more lenient
• 12/15/12: Dosage adjustment tables updated; Coverage exceptions may be made if pt is contrainindicated to the use of a TNF-inhibitor first
• 6/2013: Addition of polyarticular juvenile idiopathic arthritis induction per new FDA approval
• 12/15/13: Specific maximum approvable quantities outlined for each diagnosis; Requirement to test for latent Tb infection prior to initiation added
• 3/15/14: Policy pertains to pharmacy benefit; addition of step therapy for pharmacy benefit; allowance for 1 year authorizations
• 8/1/14: Coverage for the treatment of RA under the medical benefit requires use of Remicade or Simponi Aria first.
• 1/1/15: no policy changes
• 7/1/15: formulary distinctions updated
• 10/1/15: removal of ICD9 codes for policy
• 3/15/16: no policy changes
• 1/1/17: clinical criteria condensed to no longer require laboratory parameters; Actemra is a preferred medication
• for the treatment of RA on the pharmacy benefit; specialist requirement clarified
• 5/1/17: step therapy criteria added
• 4/2/18: addition of new indications GCA and CRS per FDA approval
• 12/13/18: addition of step for the PJIA indication under pharmacy benefit
• 2/15/19: updated age and quantity limitations

IX. References


*These guidelines are not applicable to benefits covered under Medicare Advantage. Medicare Advantage benefit coverage requests are reviewed in accordance with the guidance set forth in Chapter 15 Section 50 of the Centers for Medicare & Medicaid Services Medicare Benefit Policy Manual.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.