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Tocilizumab Intravenous

(Actemra®) J3262 (1mg)

Covered with prior authorization

Requests for Actemra® (tocilizumab intravenous) may be approved if the following criteria are met for their respective diagnoses:

- Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) OR cytokine release syndrome (CRS) associated with COVID-19.
- Inflammatory Arthritis Associated with Checkpoint Inhibitor Therapy and **ALL** of the following:
    - Documented failure or intolerance, contraindication per FDA label, intolerance, or not a candidate for ONE steroid (e.g., methylprednisolone, prednisone).
    - Individual developed inflammatory arthritis while receiving a checkpoint inhibitor (e.g., Keytruda (pembrolizumab IV infusion), Opdivo (nivolumab IV infusion), Yervoy (ipilimumab IV infusion), Tecentriq (atezolizumab IV infusion), Bavencio (avelumab IV infusion), Imfinzi (durvalumab IV infusion)).
    - Prescribed by, or in consultation with a rheumatologist or an oncologist.
- Polyarticular Juvenile Idiopathic Arthritis (PJIA) and **ALL** of the following:
    - Individual is 2 years of age or older.
    - The individual has tried and had an inadequate response to ONE conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA for at least 3-months; **OR**
    - The individual has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of PJIA; **OR**
    - The individual has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of PJIA**; OR**
    - The individual's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence, or NCCN compendium recommended use 1 or 2a for the treatment of PJIA.
    - Prescribed by, or in consultation with a rheumatologist or a prescriber who specializes in PJIA.
- Rheumatoid arthritis and **BOTH** of the following:
    - Documented failure or inadequate response, contraindication per FDA label, intolerance, or not a candidate for ONE disease-modifying anti-rheumatic drug (DMARD) (e.g., methotrexate, leflunomide, sulfasalazine)*****
      ***NOTE**: An exception to this requirement can be made if the individual has already tried a biologic. These individuals are not required to "step back" and try a DMARD.

- Prescribed by, or in consultation with, a rheumatologist or a prescriber who specializes in rheumatoid arthritis.

- Still's Disease and **ALL** of the following:
  - Documented failure or intolerance, contraindication per FDA label, intolerance, or not a candidate to ONE corticosteroid (e.g., prednisone.)*****
  - Documented failure or intolerance, contraindication per FDA label, intolerance, or not a candidate to ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) (e.g., methotrexate) given for at least 2 months.*****
    ***NOTE**: An exception to this requirement can be made if the individual has already tried a biologic. These individuals are not required to "step back" and try a steroid or a conventional synthetic DMARD.
  - Prescribed by, or in consultation with a rheumatologist or a prescriber who specializes in Still's Disease.

- Systemic Juvenile Idiopathic Arthritis (SJIA) and the following:
  - Prescribed by, or in consultation with a rheumatologist or a prescriber who specializes in Systemic Juvenile Idiopathic Arthritis (SJIA); **AND**
  - The individual has tried and had an inadequate response to at least ONE NSAID (e.g., ibuprofen, celecoxib) used in the treatment of SJIA for at least 1-month; **OR**
  - The individual has an intolerance or hypersensitivity to NSAIDs used in the treatment of SJIA; **OR**
  - The individual has an FDA labeled contraindication to NSAIDs used in the treatment of SJIA; **OR**
  - The individual has tried and had an inadequate response to another conventional agent (i.e., methotrexate, leflunomide, systemic corticosteroids) used in the treatment of SJIA for at least 3-months; **OR**
  - The individual has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of SJIA; **OR**
  - The individual has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of SJIA; **OR**
  - The individual's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence, or NCCN compendium recommended use 1 or 2a for the treatment of SJIA.

For Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) OR cytokine release syndrome (CRS) associated with COVID-19, authorization is for 1 week (4 doses only).

For all other covered uses, initial authorization and reauthorization is up to 12 months.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based

literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Requests for Actemra® (tocilizumab intravenous)may **not** be approved if the above criteria are not met and for all other indications not included above.

Annual reauthorizations will require medical chart documentation that the patient has been seen within the past 12 months and that markers of disease are improved by therapy.

Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Exclusion criteria:

- **Excluded from medical benefit review if request is for self administration.**
- Concomitant use with any other biologic including all non-tumor necrosis factor (non-TNF) biologics, anti-TNF biologics, or oral immunomodulatory agents (for example, Otezla or Xeljanz/ Xeljanz XR).
- Crohn's Disease.
- Tuberculosis, other active serious infections or a history of recurrent infections.
- If initiating therapy, individual has not had a tuberculin skin test (TST) or a Centers for Disease Control (CDC-) and Prevention -recommended equivalent to evaluate for latent tuberculosis (unless switching therapy from another targeted immune modulator and no new risk factors) [in the setting of non-emergent use only].
- It is recommended that Actemra® not be initiated in patients with an absolute neutrophil count (ANC) below 2000 per mm3, platelet count below 100,000 per mm3, or who have ALT or AST above 1.5 times the upper limit of normal (ULN).
- Doses, durations, or dosing intervals that exceed FDA maximum limits for any FDA-approved indication or are not supported by industry-accepted practice guidelines or peer-reviewed literature for the relevant off-label use.
- Individuals with significant known risk factors unless the record provides an assessment of clinical benefit that outweighs the risk.

U.S. Food and Drug Administration:
This section is to be used for informational purposes. FDA approval alone is not a basis for coverage. Targeting IL-6 is a therapeutic option for treatment of chronic inflammatory diseases such as RA. (Schoels, 2013) IL-6 has been shown to be involved in diverse physiological processes and is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as RA. Actemra® is an IL-6 receptor monoclonal antibody that binds to soluble and membrane-bound IL-6 receptors and has been shown to inhibit IL-6-mediated signaling through these receptors.1 In CRS (reported in 79% to 94% of patients receiving CAR T therapy), there are high levels of IL-6; therefore, IL-6 signaling is inhibited with Actemra® IV. (Actemra® Prescribing Information, 2018, Yescarta Prescribing Information, 2017, Kymriah Prescribing Information, 2017, Lee, 2014, NCCN/ASCO, 2019).

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Key References Accessed 8/2022:

1. Actemra® injection for intravenous infusion [prescribing information]. South San Francisco, CA: Genentech.
2. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res (Hoboken). 2011;63(4):465-482.
3. 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.
4. 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.
5. Iwamoto M, Nara H, Hirata D, et al. Humanized monoclonal anti-interleukin-6 receptor antibody for treatment of intractable adult-onset Still's disease. Arthritis Rheum. 2002;46(12):3388-3389.
6. McEvoy GK, ed. AHFS 2019 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc. 2019.
7. NCCN/ASCO Management of Immunotherapy-Related Toxicities (Immune Checkpoint Inhibitor-Related Toxicities) Clinical Practice Guidelines in Oncology National Comprehensive Cancer Network, Inc.
8. Yoshimura M, Makiyama J, Koga T, et al. Successful treatment with tocilizumab in a patient with refractory adult-onset Still's disease (AOSD). Clin Exp Rheumatol. 2010;28(1):141-142.

Date	Summary of Changes
August 2022	Criteria for use summary developed by the Ascension Medical Specialty Prior Authorization Team.
September 2022	Criteria for use summary approved by the Ascension Ambulatory Care Expert Review Panel.
October 2022	Criteria for use summary approved by the Ascension Therapeutic Affinity Group.

If you have questions, call 833-980-2352 to speak to a member of the Ascension Rx prior authorization team, or email your questions to smarthealthspecialty@ascension.org.