Clinical Policy: Tocilizumab (Actemra)

Reference Number: IN.PHAR.263
Effective Date: 07.01.16
Last Review Date: 08.21
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Tocilizumab (Actemra®) is an interleukin 6 (IL-6) receptor antagonist.

FDA Approved Indication(s)

Actemra is indicated for the treatment of:

- Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs)
- Adult patients with giant cell arteritis (GCA)
- Slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD)
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (PJIA)
- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis (SJIA)
- Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS)

Emergency Use Authorization

The U.S. Food and Drug Administration (FDA) has issued an emergency use authorization (EUA) for the emergency use of Actemra for the treatment of coronavirus disease 2019 (COVID-19) in hospitalized adults and pediatric patients (2 years of age and older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). However, Actemra is not FDA-approved for this use.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Actemra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cytokine Release Syndrome (must meet all):
1. Request is for IV formulation;
2. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg per infusion for up to 4 total doses;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Giant Cell Arteritis (must meet all)**:**

1. Request is for SC formulation;
2. Failure of a ≥ 3 consecutive month trial of a systemic corticosteroid at up to maximally tolerated doses in conjunction with MTX or azathioprine, unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 162 mg every week.

Approval duration: 12 months

C. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of PJIA as evidenced by ≥ 5 joints with active arthritis;
2. Dose does not exceed one of the following (*see Appendix E for dose rounding guidelines*) (a or b):
   a. Weight < 30 kg: 10 mg/kg IV every 4 weeks or 162 mg SC every 3 weeks;
   b. Weight ≥ 30 kg: 8 mg/kg IV every 4 weeks or 162 mg SC every 2 weeks.

Approval duration: 12 months

D. Rheumatoid Arthritis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of at least ONE conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
2. Failure of at least one of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: Enbrel, Kevzara®, Xeljanz/Xeljanz XR;
   **Prior authorization may be required for Enbrel, Kevzara, and Xeljanz/Xeljanz XR*
3. Dose does not exceed one of the following (a or b):
   a. IV: 800 mg every 4 weeks;
   b. SC: 162 mg every week.

Approval duration: 12 months

E. Systemic Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of SJIA;
2. Dose does not exceed one of the following (a or b):
   a. IV (*see Appendix E for dose rounding guidelines*):
      i. Weight < 30 kg: 12 mg/kg every 2 weeks;
      ii. Weight ≥ 30 kg: 8 mg/kg every 2 weeks;
   b. SC:

i. Weight < 30 kg: 162 mg every 2 weeks;
ii. Weight ≥ 30 kg: 162 mg every week.

Approval duration: 12 months

F. Systemic Sclerosis –Associated Interstitial Lung Disease (must meet all):
1. Request is for SC formulation;
2. Dose does not exceed 162 mg every week.

Approval duration: 12 months

G. Castleman's Disease (off-label) (must meet all)**:**
1. Diagnosis of Castleman's disease;
2. Disease is relapsed/refractory or progressive;
3. Member is human immunodeficiency virus (HIV)-negative and human herpesvirus 8 (HHV-8)-negative;
4. Prescribed as second-line therapy as a single agent;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 8 mg/kg per infusion every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

H. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Other Indications in Section I (must meet all)**:**
1. History of the requested agent within the past 90 days
2. If request is for a dose increase, new dose does not exceed one of the following (a, b, c, d, e, f):
   a. CRS: 800 mg per infusion for up to 4 doses total, or dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*);
   b. PJIA (*see Appendix E for dose rounding guidelines*) (i or ii):
      i. Weight < 30 kg: 10 mg/kg IV every 4 weeks or 162 mg SC every 3 weeks;
      ii. Weight ≥ 30 kg: 8 mg/kg IV every 4 weeks or 162 mg SC every 2 weeks;
   c. RA (i or ii):
      i. IV: 800 mg every 4 weeks;
      ii. SC: 162 mg every week;
   d. GCA, SSc-ILD: 162 mg SC every week;
   e. SJIA (*see Appendix E for dose rounding guidelines*): (i or ii):
      i. Weight < 30 kg: 12 mg/kg IV every 2 weeks 162 mg SC 2 every week;
      ii. Weight ≥ 30 kg: 8 mg/kg IV every 2 weeks or 162 mg SC every week;
   f. Castleman's Disease (i or ii):*

i. Dose does not exceed 8 mg/kg per infusion every 2 weeks;
ii. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CAR: chimeric antigen receptor
CDAI: clinical disease activity index
cJADAS: clinica juvenile arthritis disease activity score
CRS: cytokine release syndrome
DLCO: carbon monoxide diffusing capacity
DMARDs: disease-modifying anti-rheumatic drugs
FDA: Food and Drug Administration
FVC: forced vital capacity
GCA: giant cell arteritis
GI: gastrointestinal
HHV-8: human herpesvirus 8
HIV: human immunodeficiency virus
IL-6: interleukin 6
MTX: methotrexate
PJIA: polyarticular juvenile idiopathic arthritis
RA: rheumatoid arthritis
RAPID3: routine assessment of patient index data 3
SJIA: systemic juvenile idiopathic arthritis
SSc-ILD: systemic sclerosis-associated interstitial lung disease

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan®, Imuran®)	**RA** 1 mg/kg/day PO QD or divided BID **GCA*** 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
corticosteroids	**GCA*, SJIA*** Various	Various
Cuprimine® (d-penicillamine)	**RA*** Initial dose:	1,500 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD	
Cyclophosphamide (Cytoxan®, Neosar®)	**SSc-ILD*** PO: 1 – 2 mg/kg/day IV: 600 mg/m^2/month	PO: 2 mg/kg/day IV: 600 mg/m^2/month
cyclosporine (Sandimmune®, Neoral®)	**RA** 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
hydroxychloroquine (Plaquenil®)	**RA*** Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	600 mg/day
leflunomide (Arava®)	**PJIA*** Weight < 20 kg: 10 mg every other day Weight 20 - 40 kg: 10 mg/day Weight > 40 kg: 20 mg/day **RA** 100 mg PO QD for 3 days, then 20 mg PO QD **SJIA*** 100 mg PO every other day for 2 days, then 10 mg every other day	PJIA, RA: 20 mg/day SJIA: 10 mg every other day
methotrexate (Rheumatrex®)	**GCA*** 20 – 25 mg/week PO **PJIA*** 10 – 20 mg/m^2/week PO, SC, or IM **RA** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week **SJIA*** 0.5-1 mg/kg/week PO	30 mg/week
mycophenolate mofetil (CellCept®)	**SSc-ILD*** PO: 1 – 3 g/day	3 g/day
Ridaura® (auranofin)	**RA** 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine®)	**PJIA*** 30-50 mg/kg/day PO divided BID	PJIA: 2 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	RA 2 g/day PO in divided doses	RA: 3 g/day
Enbrel® (etanercept)	**PJIA** Weight < 63 kg: 0.8 mg/kg SC once weekly Weight ≥ 63 kg: 50 mg SC once weekly **RA** 25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
Kevzara® (sarilumab)	**RA** 200 mg SC once every two weeks	200 mg/2 weeks
Xeljanz® (tofacitinib)	**PJIA** • 10 kg ≤ body weight < 20 kg: 3.2 mg (3.2 mL oral solution) PO BID • 20 kg ≤ body weight < 40 kg: 4 mg (4 mL oral solution) PO BID • Body weight ≥ 40 kg: 5 mg PO BID **RA** 5 mg PO BID	10 mg/day
Xeljanz XR® (tofacitinib extended-release)	**RA** 11 mg PO QD	11 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): known hypersensitivity to Actemra
- Boxed warning(s): risk of serious infections

Appendix D: General Information
- Definition of failure of MTX or DMARDs
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness

- Improvement in ESR/CRP levels
- Improvements in activities of daily living

Appendix E: Dose Rounding Guidelines for PJIA and SJIA

Weight-based Dose Range	Vial Quantity Recommendation
≤ 83.99 mg	1 vial of 80 mg/4 mL
84 to 209.99 mg	1 vial of 200 mg/10 mL
210 to 419.99 mg	1 vial of 400 mg/20 mL
420 to 503.99 mg	1 vial of 80 mg/4 mL and 1 vial 400 mg/20 mL
504 to 629.99 mg	1 vial of 200 mg/10 mL and 1 vial 400 mg/20 mL
630 to 839.99 mg	2 vials 400 mg/20 mL
840 to 923.99 mg	1 vial of 80 mg/4 mL and 2 vials 400 mg/20 mL
924 to 1,049.99 mg	1 vial of 200 mg/10 mL and 2 vials 400 mg/20 mL
1050 to 1,259.99 mg	3 vials 400 mg/20 mL

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CRS	Weight < 30 kg: 12 mg/kg IV per infusion Weight ≥ 30 kg: 8 mg/kg IV per infusion If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses of Actemra may be administered. The interval between consecutive doses should be at least 8 hours.	IV: 800 mg/infusion, up to 4 doses
GCA	162 mg SC every week (every other week may be given based on clinical considerations)	SC: 162 mg every week
PJIA	• Weight < 30 kg: 10 mg/kg IV every 4 weeks or 162 mg SC every 3 weeks • Weight ≥ 30 kg: 8 mg/kg IV every 4 weeks or 162 mg SC every 2 weeks *See Appendix E for dose rounding guidelines*	IV: 10 mg/kg every 4 weeks SC: 162 mg every 2 weeks
RA	IV: 4 mg/kg every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response SC: Weight < 100 kg: 162 mg SC every other week, followed by an increase to every week based on clinical response Weight ≥ 100 kg: 162 mg SC every week	IV: 800 mg every 4 weeks SC: 162 mg every week
SJIA	IV: Weight < 30 kg: 12 mg/kg IV every 2 weeks Weight ≥ 30 kg: 8 mg/kg IV every 2 weeks *See Appendix E for dose rounding guidelines*	IV: 12 mg/kg every 2 weeks SC: 162 mg every week

Indication	Dosing Regimen	Maximum Dose
	SC: Weight < 30 kg: 162 mg SC every 2 weeks Weight ≥ 30 kg: 162 mg SC every week	
SSc-ILD	162 mg SC once weekly	SC: 162 mg every week

V. Product Availability

- Single-use vial: 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL
- Single-dose prefilled syringe: 162 mg/0.9 mL
- Single-dose prefilled autoinjector: 162 mg/0.9 mL

VI. References

1. Actemra Prescribing Information. South San Francisco, CA: Genentech; March 2021. Available at: https://www.actemra.com/. Accessed June 30, 2021.
2. Actemra. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 15, 2021.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: https://www.clinicalpharmacology-ip.com/.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3262	Injection, tocilizumab, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
PA Criteria alignment with FFS	08/21	OMPP Approved

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.