Clinical Policy: Tocilizumab (Actemra)

Reference Number: CP.PHAR.263
Effective Date: 07/16
Last Review Date: 07/17
Line of Business: Medicaid

Revision Log

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

Description

Tocilizumab (Actemra®) is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody.

FDA approved indication

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 antirheumatic drugs (DMARDs)
- 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)
- Adult patients with giant cell arteritis (GCA)

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) 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. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of PJIA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
   a. Failure of methotrexate (MTX) for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX, failure of sulfasalazine or leflunomide for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of etanercept *(Enbrel is preferred)* AND adalimumab *(Humira is preferred),* each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
6. Tuberculosis (TB) test within the past 12 months is negative, or if positive, active TB has been ruled out and the patient has received treatment for latent TB infection;
7. Prescribed route of administration is intravenous (IV) infusion;
8. Dose does not exceed 10 mg/kg once every 4 weeks.

Approval duration: 6 months

B. Systemic Juvenile Idiopathic Arthritis(must meet all)**:**
1. Diagnosis of SJIA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Failure of one of the following therapies (a or b), unless all are contraindicated or clinically significant adverse effects are experienced:
   a. A non-steroidal anti-inflammatory drug for 1 month and a corticosteroid for 2 weeks;
   b. MTX or leflunomide for ≥ 3 consecutive months;
5. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the patient has received treatment for latent TB infection;
6. Prescribed route of administration is IV infusion;
7. Dose does not exceed 12 mg/kg once every 2 weeks.

Approval duration: 6 months

C. Rheumatoid Arthritis (must meet all)**:**
1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (refer to Appendix B);
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of MTX for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX, failure of sulfasalazine, leflunomide, or hydroxychloroquine for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of etanercept *(Enbrel is preferred)* AND adalimumab *(Humira is preferred)*, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
6. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the patient has received treatment for latent TB infection;
7. Dose does not exceed the following:
   a. IV: 800mg every 4 weeks;
   b. Subcutaneous (SC): 162mg every week.

Approval duration: 6 months

D. Giant Cell Arteritis (must meet all)**:**
1. Diagnosis of GCA;
2. Prescribed by or in consultation with a rheumatologist;
3. Failure of at least a 12-week trial of a corticosteroid (at up to maximally tolerated doses) in conjunction with MTX or azathioprine, unless contraindicated or clinically significant adverse effects are experienced;

4. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the patient has received treatment for latent TB infection;
5. Dose does not exceed 162 mg SC every week.

Approval duration: 6 months

E. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy (e.g. labs, sign/symptom reduction, no significant toxicity);
3. If request is for a dose increase, new dose does not exceed the following (a, b, c, or d):
   a. For PJIA: 10 mg/kg IV once every 4 weeks;
   b. For SJIA: 12 mg/kg IV once every 2 weeks;
   c. For RA (i or ii):
      i. IV: 800mg every 4 weeks;
      ii. SC: 162 mg every week;
   d. For GCA: 162 mg SC every week.

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 CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACPA: anti-citrullinated protein antibody
ALT: alanine aminotransferase
ANC: absolute neutrophil count
AST: aspartate aminotransferase
CCP: citrullinated peptide
CRP: C-reactive protein
DMARDs: disease-modifying antirheumatic drugs
ESR: erythrocyte sedimentation rate
FDA: Food and Drug Administration
GCA: giant cell arteritis
IL: interleukin
IV: intravenous

PJIA: polyarticular juvenile idiopathic arthritis
RA: rheumatoid arthritis
RF: rheumatoid factor
SC: subcutaneous
SJIA: systemic juvenile idiopathic arthritis
TB: tuberculosis
TNF: tumor necrosis factor
ULN: upper limit of normal

Appendix B: The 2010 ACR Classification Criteria for RA
Add score of categories A through D. A score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	**Joint involvement**	Score
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5
B	**Serology (at least one test result is needed for classification)**	
	Negative rheumatoid factor (RF) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA * *Low: < 3 x upper limit of normal*	2
	High positive RF *or* high positive ACPA * *High: ≥ 3 x upper limit of normal*	3
C	**Acute phase reactants (at least one test result is needed for classification)**	
	Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
	Abnormal CRP or normal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix C: Definition of MTX or DMARD Failure
In RA, failure of MTX or DMARD is defined as ≤ 50% decrease in swollen joint count, ≤ 50% decrease in tender joint count, and ≤ 50% decrease in ESR, or ≤ 50% decrease in CRP.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Rheumatoid arthritis	IV: 4 mg/kg every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response SC: patients <100 kg: 162 mg SC every other week, followed by an increase to every week based on clinical response Patients >100 kg: 162 mg SC every week	IV: 800 mg every 4 weeks SC: 162 mg every week

Indication	Dosing Regimen	Maximum Dose
Polyarticular juvenile idiopathic arthritis	Patients < 30 kg: 10 mg/kg IV every 4 weeks Patients > 30 kg: 8 mg/kg IV every 4 weeks	IV: 10 mg/kg every 4 weeks
Systemic juvenile idiopathic arthritis	Patients < 30 kg: 12 mg/kg IV every 2 weeks Patients > 30 kg: 8 mg/kg IV every 2 weeks	IV: 12 mg/kg every 2 weeks
Giant Cell arthritis	162 mg SC once every week in combination with a tapering course of glucocorticoids A dose of 162 mg SC every other week may be prescribed based on clinical considerations.	SC: 162 mg every week

VI. Product Availability

Single-use vials for IV administration: 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL
Prefilled syringe for SC administration: 162 mg/0.9 mL

VIII. References

1. Actemra Prescribing Information. South San Francisco, CA: Genentech; November 2014. Available at https://www.actemra.com/. Accessed June 22, 2017.
2. Ringold, S., Weiss, P. F., Beukelman, T., DeWitt, E. M., Ilowite, N. T., Kimura, Y., Laxer, R. M., Lovell, D. J., Nigrovic, P. A., Robinson, A. B. and Vehe, R. K. (2013), 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications. Arthritis & Rheumatism, 65: 2499–2512.
3. European League Against Rheumatism. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2009;68:318–323.
4. Aletaha D, Neogi T, Silman AJ et al. 2010 Rheumatoid Arthritis Classification Criteria. Arthritis and Rheumatism September 2010;62(9):2569-2581.

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.86.Arthritis Treatments PJIA, SJIA and RA: Removed criteria related to HBV, malignant disease, concomitant use with other biologics, and concurrent administration of live vaccines; added dosing requirements. PJIA: removed question related to number of affected joints; modified criteria to require trial of MTX, unless contraindicated; added sulfasalazine as an alternative to MTX is contraindicated; added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated; SJIA: removed question related to active systemic features; modified duration of treatment of NSAIDs and corticosteroids to for ≥ 1 month and ≥ 2 weeks, respectively; added MTX or leflunomide as an option for failure; added requirement specifying route of administration per PI.	06/16	07/16

Reviews, Revisions, and Approvals	Date	Approval Date
RA: changed age requirement to 18 years per PI/FDA labeling; modified criteria to require trial of methotrexate, unless contraindicated; added sulfasalazine and hydroxychloroquine as alternatives to methotrexate if methotrexate is contraindicated; added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated; Re-auth: combined into All Indications; added dosing and reasons to discontinue. Modified approval duration to 6 months for initial and 12 months for renewal;		
Policy converted to new template. Added criteria for new FDA indication Giant Cell Arteritis. Revised criteria for confirmation of RA diagnosis per 2010 ACR Criteria. Removed safety requirements per updated CPAC Safety Precaution in PA Policies approach.	07/17	07/17

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.

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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.

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