Clinical Policy: Tocilizumab (Actemra)

Reference Number: PA.CP.PHAR.263
Effective Date: 01/18
Last Review Date: 07/17
Line of Business: Medicaid

Revision Log

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 Pennsylvania Health and Wellness® 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 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 PA.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 Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to PA.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 – PA.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
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

Indication	Dosing Regimen	Maximum Dose
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