Clinical Policy: Tocilizumab (Actemra)
Reference Number: CP.PHAR.263
Effective Date: 07.01.16
Last Review Date: 08.21
Line of Business: Medicaid

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. Coronavirus-19 Infection (FDA Emergency Use Authorization):
      1. Initiation of outpatient treatment will not be authorized as Actemra is authorized for emergency use only in the hospitalized setting (see Appendix K).
      Approval duration: Not Applicable
B. Cytokine Release Syndrome (must meet all):
   1. Request is for IV formulation;
   2. Age ≥ 2 years;
   3. Member meets one of the following (a or b):
      a. Member has a scheduled CAR T cell therapy (e.g., Kymriah™, Yescarta™);
      b. Member has developed refractory (i.e., inadequate response to steroids, vasopressors) CRS related to blinatumomab therapy;
   4. 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: Up to 4 doses total

C. Giant Cell Arteritis (must meet all):
   1. Diagnosis of GCA;
   2. Request is for SC formulation;
   3. Prescribed by or in consultation with a rheumatologist;
   4. Age ≥ 18 years;
   5. 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;
   6. Dose does not exceed 162 mg every week.

Approval duration: 6 months

D. Polyarticular Juvenile Idiopathic Arthritis (must meet all):
   1. Diagnosis of PJIA as evidenced by ≥ 5 joints with active arthritis;
   2. Prescribed by or in consultation with a rheumatologist;
   3. Age ≥ 2 years;
   4. Documented baseline 10-joint clinical juvenile arthritis disease activity score (cJADAS-10) (see Appendix I);
   5. Member meets one of the following (a, b, c, or d):
      a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;
      b. If intolerance or contraindication to MTX (see Appendix D), failure of a ≥ 3 consecutive month trial of leflunomide or sulfasalazine at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
      c. For sacroiliitis/axial spine involvement (i.e., spine, hip), failure of a ≥ 4 week trial of an NSAID at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      d. Documented presence of high disease activity as evidenced by a cJADAS-10 > 8.5 (see Appendix I);
   6. Failure of both of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated: Enbrel®, Xeljanz®.

*Prior authorization may be required for Enbrel and Xeljanz
7. 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: 6 months

E. Rheumatoid Arthritis (must meet all):
1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (see Appendix F);
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 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;
5. Failure of at least TWO 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
6. Documentation of one of the following baseline assessment scores (a or b):
   a. Clinical disease activity index (CDAI) score (see Appendix G);
   b. Routine assessment of patient index data 3 (RAPID3) score (see Appendix H);
7. 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: 6 months

F. Systemic Juvenile Idiopathic Arthritis (must meet all):
1. Diagnosis of SJIA;
2. Prescribed by or in consultation with a dermatologist, rheumatologist, or gastroenterologist;
3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX or leflunomide at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Failure of a ≥ 2-week trial of a systemic corticosteroid at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. 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: 6 months

G. Systemic Sclerosis –Associated Interstitial Lung Disease (must meet all):
   1. Diagnosis of SSc-ILD;
   2. Request is for SC formulation;
   3. Prescribed by or in consultation with a pulmonologist or rheumatologist;
   4. Member meets both of the following (a and b):
      a. Pulmonary fibrosis on high-resolution computed tomography (HRCT);
      b. Additional signs of SSc are identified (see Appendix J);
   5. Failure of a ≥ 3 consecutive month trial of cyclophosphamide or mycophenolate mofetil, at up to maximally indicated doses, unless both are contraindicated or clinically significant adverse effects are experienced;
   6. Baseline forced vital capacity (FVC) ≥ 40% of predicted;
   7. Baseline carbon monoxide diffusing capacity (DLCO) ≥ 30% of predicted;
   8. Dose does not exceed 162 mg every week.

Approval duration: 6 months

H. 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: 6 months

I. 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. Coronavirus-19 Infection (FDA Emergency Use Authorization):
      1. Continuation of therapy in the outpatient setting will not be authorized as Actemra is authorized for emergency use only in the hospitalized setting as a single dose, with an optional second dose (see Appendix K).

Approval duration: Not Applicable
A. All Other Indications in Section I (must meet all):
   1. Member meets one of the following (a or b):
      a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      b. Documentation supports that member is currently receiving Actemra IV for CAR T cell-induced CRS and member has not yet received 4 doses total;
   2. Member meets one of the following (a, b, or c):
      a. For RA: member is responding positively to therapy as evidenced by one of the following (i or ii):
         i. A decrease in CDAI (see Appendix G) or RAPID3 (see Appendix H) score from baseline;
         ii. Medical justification stating inability to conduct CDAI re-assessment, and submission of RAPID3 score associated with disease severity that is similar to initial CDAI assessment or improved;
      b. For pJIA, member is responding positively to therapy as evidenced by a decrease in cJADAS-10 from baseline (see Appendix I);
      c. For all other indications: member is responding positively to therapy;
   3. 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:
   CRS: Up to 4 doses total
   All other indications: 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. 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 policies – CP.PMN.53 for Medicaid or evidence of coverage documents;
B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia®, Enbrel®, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz®/Xeljanz® XR, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, and Rituxan Hycela®], selective co-stimulation modulators [Orencia®], or integrin receptor antagonists [Entyvio®] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

IV. 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 antirheumatic 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>azathioprine</td>
<td>RA</td>
<td>2.5 mg/kg/day</td>
</tr>
<tr>
<td>(Azasan®, Imuran®)</td>
<td>1 mg/kg/day PO QD or divided BID</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GCA*</td>
<td></td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/ Maximum Dose</td>
</tr>
<tr>
<td>-----------</td>
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<td>--------------------------</td>
</tr>
<tr>
<td>corticosteroids</td>
<td>GCA*, SJIA* Various</td>
<td>Various</td>
</tr>
<tr>
<td>Cuprimine® (d-penicillamine)</td>
<td>RA* Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD</td>
<td>1,500 mg/day</td>
</tr>
<tr>
<td>Cyclophosphamide (Cytoxan®, Neosar®)</td>
<td>SSc-ILD* PO: 1 – 2 mg/kg/day IV: 600 mg/m²/month</td>
<td>PO: 2 mg/kg/day IV: 600 mg/m²/month</td>
</tr>
<tr>
<td>cyclosporine (Sandimmune®, Neoral®)</td>
<td>RA 2.5 – 4 mg/kg/day PO divided BID</td>
<td>4 mg/kg/day</td>
</tr>
<tr>
<td>hydroxychloroquine (Plaquenil®)</td>
<td>RA* Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD</td>
<td>600 mg/day</td>
</tr>
<tr>
<td>leflunomide (Arava®)</td>
<td>PJIA* Weight &lt; 20 kg: 10 mg every other day Weight 20 - 40 kg: 10 mg/day Weight &gt; 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</td>
<td>PJIA, RA: 20 mg/day SJIA: 10 mg every other day</td>
</tr>
<tr>
<td>methotrexate (Rheumatrex®)</td>
<td>GCA* 20 – 25 mg/week PO PJIA* 10 – 20 mg/m²/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</td>
<td>30 mg/week</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
</tr>
<tr>
<td>-----------</td>
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<td>------------------------</td>
</tr>
<tr>
<td>mycophenolate mofetil (CellCept®)</td>
<td>SSc-ILD* PO: 1 – 3 g/day</td>
<td>3 g/day</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ridaura® (auranofin)</td>
<td>RA 6 mg PO QD or 3 mg PO BID</td>
<td>9 mg/day (3 mg TID)</td>
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<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>sulfasalazine (Azulfidine®)</td>
<td>RA 2 g/day PO in divided doses</td>
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<td></td>
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<td></td>
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<tr>
<td>Enbrel® (etanercept)</td>
<td>RA 25 mg SC twice weekly or 50 mg SC once weekly</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PJIA Weight &lt; 63 kg: 0.8 mg/kg SC once weekly</td>
<td>50 mg/week</td>
</tr>
<tr>
<td></td>
<td>Weight ≥ 63 kg: 50 mg SC once weekly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RA 200 mg SC once every two weeks</td>
<td>200 mg/2 weeks</td>
</tr>
<tr>
<td>Kevzara® (sarilumab)</td>
<td>RA 200 mg SC once every two weeks</td>
<td>200 mg/2 weeks</td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xeljanz® (tofacitinib)</td>
<td>RA 5 mg PO BID</td>
<td>10 mg/day</td>
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<tr>
<td></td>
<td>10 kg ≤ body weight &lt; 20 kg: 3.2 mg (3.2 mL oral solution) PO BID</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 kg ≤ body weight &lt; 40 kg: 4 mg (4 mL oral solution) PO BID</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Body weight ≥ 40 kg: 5 mg PO BID</td>
<td></td>
</tr>
<tr>
<td>Xeljanz XR® (tofacitinib extended-release)</td>
<td>RA 11 mg PO QD</td>
<td>11 mg/day</td>
</tr>
</tbody>
</table>

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.

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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

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

### Appendix F: 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.

<table>
<thead>
<tr>
<th><strong>A</strong> Joint involvement</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 large joint</td>
<td>0</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
</tr>
<tr>
<td>1-3 small joints (with or without involvement of large joints)</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints (with or without involvement of large joints)</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 10 joints (at least one small joint)</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>B</strong> Serology (at least one test result is needed for classification)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative rheumatoid factor (RF) and negative anti-citrullinated protein antibody (ACPA)</td>
<td>0</td>
</tr>
<tr>
<td>Low positive RF or low positive ACPA</td>
<td>2</td>
</tr>
<tr>
<td>* Low: &lt; 3 x upper limit of normal</td>
<td></td>
</tr>
<tr>
<td>High positive RF or high positive ACPA</td>
<td>3</td>
</tr>
<tr>
<td>* High: ≥ 3 x upper limit of normal</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>C</strong> Acute phase reactants (at least one test result is needed for classification)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP or abnormal ESR</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>D</strong> Duration of symptoms</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥ 6 weeks</td>
<td>1</td>
</tr>
</tbody>
</table>
Appendix G: Clinical Disease Activity Index (CDAI) Score
The Clinical Disease Activity Index (CDAI) is a composite index for assessing disease activity in RA. CDAI is based on the simple summation of the count of swollen/tender joint count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity. The CDAI score ranges from 0 to 76.

<table>
<thead>
<tr>
<th>CDAI Score</th>
<th>Disease state interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2.8</td>
<td>Remission</td>
</tr>
<tr>
<td>&gt; 2.8 to ≤ 10</td>
<td>Low disease activity</td>
</tr>
<tr>
<td>&gt; 10 to ≤ 22</td>
<td>Moderate disease activity</td>
</tr>
<tr>
<td>&gt; 22</td>
<td>High disease activity</td>
</tr>
</tbody>
</table>

Appendix H: Routine Assessment of Patient Index Data 3 (RAPID3) Score
The Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of the three patient-reported ACR core data set measures: function, pain, and patient global estimate of status. Each of the individual measures is scored 0 – 10, and the maximum achievable score is 30.

<table>
<thead>
<tr>
<th>RAPID3 Score</th>
<th>Disease state interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3</td>
<td>Remission</td>
</tr>
<tr>
<td>3.1 to 6</td>
<td>Low disease activity</td>
</tr>
<tr>
<td>6.1 to 12</td>
<td>Moderate disease activity</td>
</tr>
<tr>
<td>&gt; 12</td>
<td>High disease activity</td>
</tr>
</tbody>
</table>

Appendix I: Clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS-10)
The cJADAS10 is a continuous disease activity score specific to JIA and consisting of the following three parameters totaling a maximum of 30 points:
- Physician’s global assessment of disease activity measured on a 0-10 visual analog scale (VAS), where 0 = no activity and 10 = maximum activity;
- Parent global assessment of well-being measured on a 0-10 VAS, where 0 = very well and 10 = very poor;
- Count of joints with active disease to a maximum count of 10 active joints*

*ACR definition of active joint: presence of swelling (not due to currently inactive synovitis or to bony enlargement) or, if swelling is not present, limitation of motion accompanied by pain, tenderness, or both

<table>
<thead>
<tr>
<th>cJADAS-10</th>
<th>Disease state interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1</td>
<td>Inactive disease</td>
</tr>
<tr>
<td>1.1 to 2.5</td>
<td>Low disease activity</td>
</tr>
<tr>
<td>2.51 to 8.5</td>
<td>Moderate disease activity</td>
</tr>
<tr>
<td>&gt; 8.5</td>
<td>High disease activity</td>
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</table>

Appendix J: American College of Rheumatology (ACR) 2013 SSc Classification Criteria
While the majority of patients with SSc experience skin thickening and variable involvement of internal organs, there is no one confirmatory test for SSc. Similar to the IPF guidelines above, ACR lists HRCT as a diagnostic method for determining pulmonary fibrosis in SSc-ILD. The other diagnostic parameters below are drawn from ACR’s scoring system purposed for clinical trials. While informative, ACR cautions that the scoring system parameters are not all inclusive of the myriad of SSc manifestations that may occur across musculoskeletal, cardiovascular, renal, neuromuscular and genitourinary systems.
Examples of SSc skin/internal organ manifestations and associated laboratory tests:
- Skin thickening of the fingers
- Fingertip lesions
- Telangiectasia
- Abnormal nailfold capillaries
- Raynaud’s phenomenon
- SSc-ILD
- Pulmonary arterial hypertension
- SSc-related autoantibodies
- Anticentromere
- Anti-topoisomerase I (anti-Scl-70)
- Anti-RNA polymerase III

Appendix K: Coronavirus-19 Infection (FDA Emergency Use Authorization):
- An EUA is an FDA authorization for the emergency use of an unapproved product or unapproved use of an approved product (i.e., drug, biological product, or device) in the United States under certain circumstances including, but not limited to, when the Secretary of HHS declares that there is a public health emergency that affects the national security or the health and security of United States citizens living abroad, and that involves biological agent(s) or a disease or condition that may be attributable to such agent(s).
- The EUA was granted, given that there is no adequate, approved and available alternative to Actemra for treatment of adults and pediatric patients (2 years of age and older) hospitalized with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. For information on clinical studies of ACTEMRA and other therapies for the treatment of COVID-19.
- Actemra is authorized under an EUA as a single 60-minute intravenous infusion, with an optional additional dose if clinical signs or symptoms worsen or do not improve after the first dose.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
</table>
| 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 | IV: 10 mg/kg every 4 weeks  
SC: 162 mg every 2 weeks |

See Appendix E for dose rounding guidelines
### Indication | Dosing Regimen | Maximum Dose
--- | --- | ---
**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
SC: Weight < 30 kg: 162 mg SC every 2 weeks
Weight ≥ 30 kg: 162 mg SC every week | IV: 12 mg/kg every 2 weeks
SC: 162 mg every week
**SSc-ILD** | 162 mg SC once weekly | SC: 162 mg every week

### VI. 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

### VII. References


**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.

<table>
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<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J3262</td>
<td>Injection, tocilizumab, 1 mg</td>
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**Reviews, Revisions, and Approvals**

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SJIA: Removed requirement for trial/failure of NSAID as it not a first line therapy recommended by the SJIA guidelines.

GCA: Added age requirement as safety and efficacy have not been established in pediatric populations.

Added criteria for new indication of cytokine release syndrome

Corrected continued approval duration for “all other indications” from “6 months or member’s renewal date, whichever is longer” to 12 months

2Q 2018 annual review: policies combined for HIM and Medicaid lines of business; HIM: removed specific diagnosis requirements for RA, removed trial and failure of NSAIDs for SJIA as it is not first line; Medicaid and HIM: modified trial and failure for RA to at least one conventional DMARD, modified requirement of corticosteroid trial to be 3 consecutive months for GCS, removed TB testing for all indications, added dermatologist and GI specialist as prescriber specialists for SJIA; added age requirement for CRS; added weight-based max dosing requirements for PJIA and SJIA; references reviewed and updated.

No significant changes: newly FDA-approved subcutaneous dosing for PJIA added.
### Reviews, Revisions, and Approvals

<table>
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**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.