Clinical Policy: Tocilizumab (Actemra), Tocilizumab-anoh (Avtozma), Tocilizumab-bavi (Tofidence), Tocilizumab-aazg (Tyenne)

Reference Number: CP.PHAR.263
Effective Date: 07.01.16
Last Review Date: 11.25
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®) and its biosimilars [tocilizumab-anoh (Avtozma®), tocilizumab-bavi (Tofidence™) and tocilizumab-aazg (Tyenne®)] are interleukin 6 (IL-6) receptor antagonists.

FDA Approved Indication(s)

Actemra, Avtozma, Tofidence, and Tyenne are 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)
- 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)
- Coronavirus disease 2019 (COVID-19) in hospitalized adult (*all*) and pediatric patients aged 2 years and older (*Actemra only*) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Actemra, Avtozma, and Tyenne are also indicated for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in adults and pediatric patients 2 years of age and older.

Actemra is also indicated for the treatment of slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD).

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, Avtozma, Tofidence, and Tyenne are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Coronavirus-19 Infection:

1. Initiation of outpatient treatment will not be authorized as Actemra, Avtozma, Tofidence, and Tyenne are FDA-approved for use only in the hospitalized setting.

Approval duration: Not applicable

B. Cytokine Release Syndrome (must meet all):
1. Request is for Actemra, Avtozma, or Tyenne;
2. Request is for IV formulation;
3. Age ≥ 2 years;
4. If request is for Avtozma or Tyenne, member must use Actemra, unless contraindicated or clinically significant adverse effects are experienced;
5. Member meets one of the following (a, b, or c):
   a. Member has a scheduled CAR T cell therapy (e.g., Abecma®, Breyanzi®, Carvykti™, Kymriah™, Tecartus®, Yescarta™);
   b. Used as supportive care in severe CRS related to blinatumomab therapy;
   c. Used as prophylaxis to reduce the risk of CRS when administering teclistamab-cqyv;
6. 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. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. If request is for Avtozma, Tofidence, or Tyenne, member must use Actemra, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of a systemic corticosteroid at up to maximally tolerated doses, unless contraindicated, clinically significant adverse effects are experienced, unless previously failed a biologic agent for GCA;
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Dose does not exceed one of the following (a or b):
   a. 6 mg/kg IV every 4 weeks;
   b. Actemra, Avtozma, or Tyenne only: 162 mg SC every week.

Approval duration: 12 months

D. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**
1. Diagnosis of PJIA* as evidenced by ≥ 5 joints with active arthritis;
   **Overlap of diagnosis exists in children with JIA and non-systemic polyarthritis, which may include children from ILAR JIA categories of enthesitis-related arthritis*
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Member meets one of the following, unless previously failed a biologic agent for pJIA (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. Documentation of high disease activity;

5. If request is for Avtozma, Tofidence, or Tyenne, member meets ALL* of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c):
   a. Member must use Actemra;
   b. Failure of one adalimumab product (e.g. *Hadlima™, Simlandi®, Yusimry™, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), unless the member has had a history of failure of two TNF blockers;
   c. If member has not responded or is intolerant to one or more TNF blockers, failure of Xeljanz®, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

   **Prior authorization may be required for adalimumab products, Actemra, and Xeljanz*
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Dose does not exceed one of the following (*see Appendix E for dose rounding guidelines*) (a or b):
   a. Weight < 30 kg (i or ii):
      i. 10 mg/kg IV every 4 weeks;
      ii. Actemra, Avtozma, or Tyenne only: 162 mg SC every 3 weeks;
   b. Weight ≥ 30 kg (i or ii):
      i. 8 mg/kg IV every 4 weeks;
      ii. Actemra, Avtozma, or Tyenne only: 162 mg SC every 2 weeks.

Approval duration: 12 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, unless previously failed a biologic agent for RA (a or b):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and 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 clinically significant adverse effects are experienced or all are contraindicated;

5. If request is for Avtozma, Tofidence, or Tyenne, member meets ALL* of the following, unless clinically significant adverse effects are experienced or all are contraindicated (a, b, and c):
   a. Member must use Actemra;
   b. Failure of one adalimumab product (e.g., *Hadlima, Simlandi, Yusimry, adalimumab-aaty, adalimumab-adaz, adalimumab-adbm, and adalimumab-fkjp are preferred*), unless the member has had a history of failure of two TNF blockers;
   c. If member has not responded or is intolerant to one or more TNF blockers, failure of Xeljanz/Xeljanz XR®, unless member has cardiovascular risk and benefits do not outweigh the risk of treatment;

   **Prior authorization may be required for adalimumab products, Actemra, 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. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. Dose does not exceed one of the following (a or b):
   a. 800 mg IV every 4 weeks;
   b. Actemra, Avtozma, or Tyenne only: 162 mg SC every week.

Approval duration: 12 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. If request is for Avtozma, Tofidence, or Tyenne, member must use Actemra, unless contraindicated or clinically significant adverse effects are experienced;
5. Member meets one of the following, unless previously failed a biologic agent for sJIA (a, b, or c):
   a. Failure of an NSAID at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Failure of a ≥ 3 consecutive month trial of MTX or leflunomide at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
   c. 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;
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);

7. Dose does not exceed one of the following (a or b):
   a. One of the following (*see Appendix E for dose rounding guidelines*) (i or ii):
      i. Weight < 30 kg: 12 mg/kg IV every 2 weeks;
      ii. Weight ≥ 30 kg: 8 mg/kg IV every 2 weeks;
   b. Actemra, Avtozma, or Tyenne only (i or ii):
      i. Weight < 30 kg: 162 mg SC every 2 weeks;
      ii. Weight ≥ 30 kg: 162 mg SC every week.

Approval duration: 12 months

G. Systemic Sclerosis –Associated Interstitial Lung Disease (must meet all):
1. Diagnosis of SSc-ILD;
2. Request is for Actemra;
3. Request is for SC formulation;
4. Prescribed by or in consultation with a pulmonologist or rheumatologist;
5. 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)*;
6. 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;
7. Baseline forced vital capacity (FVC) ≥ 40% of predicted;
8. Baseline carbon monoxide diffusing capacity (DLCO) ≥ 30% of predicted;
9. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
10. Dose does not exceed 162 mg every week.

Approval duration: 12 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 has one of the following (a or b):
   a. Unicentric disease that is human immunodeficiency virus (HIV)-negative and human herpesvirus 8 (HHV-8)-negative;
   b. Multicentric disease;
4. Prescribed as second-line therapy as a single agent;
5. If request is for Avtozma, Tofidence, or Tyenne, member must use Actemra, unless contraindicated or clinically significant adverse effects are experienced;
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. 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

I. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Coronavirus-19 Infection:
1. Continuation of therapy in the outpatient setting will not be authorized as Actemra, Avtozma, Tofidence, and Tyenne are FDA-approved for use only in the hospitalized setting as a single dose, with an optional second dose.

Approval duration: Not applicable

B. All Other Indications in Section I (must meet all)**:**
1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
   c. Documentation supports that member is currently receiving IV Actemra, IV Avtozma, or IV Tyenne for CAR T cell-induced CRS and member has not yet received 4 doses total;
2. Member meets one of the following (a or b):
   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 all other indications: Member is responding positively to therapy;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);

4. If request is for a dose increase, new dose does not exceed one of the following (a, b, c, d, e, f, or g):
   a. CRS: Actemra, Avtozma, and Tyenne only: 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 (1 or 2):
         1) 10 mg/kg IV every 4 weeks;
         2) Actemra, Avtozma, or Tyenne only: 162 mg SC every 3 weeks;
      ii. Weight ≥ 30 kg (1 or 2):
         1) 8 mg/kg IV every 4 weeks;
         2) Actemra, Avtozma, or Tyenne only: 162 mg SC every 2 weeks;
   c. RA (i or ii):
      i. 800 mg IV every 4 weeks;
      ii. Actemra, Avtozma, or Tyenne only: 162 mg SC every week;
   d. GCA (i or ii):
      i. 600 mg IV every 4 weeks;
      ii. Actemra, Avtozma, or Tyenne only: 162 mg SC every week;
   e. SSc-ILD: Actemra only: 162 mg SC every week;
   f. SJIA (i or ii):
      i. One of the following (*see Appendix E for dose rounding guidelines*) (1 or 2):
         1) Weight < 30 kg: 12 mg/kg IV every 2 weeks;
         2) Weight ≥ 30 kg: 8 mg/kg IV every 2 weeks;
      ii. Actemra, Avtozma, or Tyenne only: one of the following (1 or 2):
         1) Weight < 30 kg: 162 mg SC every 2 weeks;
         2) Weight ≥ 30 kg: 162 mg SC every week;
   g. 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

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 with biological disease-modifying antirheumatic drugs (bDMARDs) or potent immunosuppressants, including but not limited to any tumor necrosis factor (TNF) antagonists [e.g., Cimzia®, Enbrel®, Humira® and its biosimilars, Remicade® and its biosimilars, Simponi®], interleukin agents [e.g., Actemra® (IL-6RA) and its biosimilars, Arcalyst® (IL-1 blocker), Bimzelx® (IL-17A and F antagonist), Cosentyx® (IL-17A inhibitor), Ilaris® (IL-1 blocker), Ilumya™ (IL-23 inhibitor), Kevzara® (IL-6RA), Kineret® (IL-1RA), Omvoh™ (IL-23 antagonist), Siliq™ (IL-17RA), Skyrizi™ (IL-23 inhibitor), Spevigo® (IL-36 antagonist), Stelara® (IL-12/23 inhibitor) and its biosimilars, Taltz® (IL-17A inhibitor), Tremfya® (IL-23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Cibinqo™, Olumiant™, Rinvoq™, Xeljanz®/Xeljanz® XR,], anti-CD20 monoclonal antibodies [Rituxan® and its biosimilars], selective co-stimulation modulators [Orencia®], integrin receptor antagonists [Entyvio®], tyrosine kinase 2 inhibitors [Sotyktu™], and sphingosine 1-phosphate receptor modulator [Velsipity™] because of the additive immunosuppression, increased risk of neutropenia, as well as increased risk of serious infections.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CAR: chimeric antigen receptor
CDAI: clinical disease activity index
cJADAS: clinical juvenile arthritis disease activity score
COVID-19: Coronavirus Disease 2019
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	2.5 mg/kg/day
corticosteroids	**GCA*, SJIA*** Various	Various
Cuprimine® (d-penicillamine)	**RA*** Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD	1,500 mg/day
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** Initial dose (for low risk hepatotoxicity or myelosuppression): 100 mg PO QD for 3 days Maintenance dose: 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 (Trexall®, Otrexup™, Rasuvo®, RediTrex®, Xatmep™, Rheumatrex®)	**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 or SC	30 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
mycophenolate mofetil (CellCept®)	**SSc-ILD*** PO: 1 – 3 g/day	3 g/day
NSAIDs (e.g., naproxen, ibuprofen, indomethacin)	**sJIA*** Varies	Varies
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 **RA** 2 g/day PO in divided doses	PJIA: 2 g/day RA: 3 g/day
Hadlima (adalimumab-bwwd), Simlandi (adalimumab-ryvk), Yusimry (adalimumab-aqvh), adalimumab-aaty (Yuflyma®), adalimumab-adaz (Hyrimoz®), adalimumab-fkjp (Hulio®), adalimumab-adbm (Cyltezo®)	**RA** 40 mg SC every other week **pJIA** **Cyltezo, Hadlima, Hyrimoz:** Weight 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg SC every other week **Cyltezo, Hadlima, Hulio, Yuflyma:** Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg SC every other week **Cyltezo, Hadlima, Hulio, Hyrimoz, Simlandi, Yuflyma, Yusimry:** Weight ≥ 30 kg (66 lbs): 40 mg SC every other week	40 mg every other week
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 tocilizumab products
- 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

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.

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 abnormal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

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.

CDAI Score	Disease state interpretation
≤ 2.8	Remission
> 2.8 to ≤ 10	Low disease activity
> 10 to ≤ 22	Moderate disease activity
> 22	High disease activity

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.

RAPID3 Score	Disease state interpretation
≤ 3	Remission
3.1 to 6	Low disease activity
6.1 to 12	Moderate disease activity
> 12	High disease activity

Appendix I: Polyarticular Juvenile Idiopathic Arthritis Disease Activity
According to 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis, disease activity (moderate/high and low) as defined by the clinical Juvenile Disease Activity score based on 10 joints (cJADAS-10) is provided as a general parameter and should be interpreted within the clinical context.
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*

cJADAS-10	Disease state interpretation
≤ 1	Inactive disease
1.1 to 2.5	Low disease activity
2.51 to 8.5	Moderate disease activity
> 8.5	High disease activity

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

V. Dosage and Administration

	Indication	Dosing Regimen	Maximum Dose
Tocilizumab (Actemra) and biosimilars (Avtozma, Tofidence, Tyenne)	PJIA	**Actemra, Avtozma, Tofidence, Tyenne:** • Weight < 30 kg: 10 mg/kg IV every 4 weeks • Weight ≥ 30 kg: 8 mg/kg IV every 4 weeks *See Appendix E for dose rounding guidelines* **Actemra, Avtozma, Tyenne:** • Weight < 30 kg: 162 mg SC every 3 weeks • Weight ≥ 30 kg: 162 mg SC every 2 weeks	IV: 10 mg/kg every 4 weeks SC: 162 mg every 2 weeks

	Indication	Dosing Regimen	Maximum Dose
	RA	**Actemra, Avtozma, Tofidence, Tyenne:** IV: 4 mg/kg every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response **Actemra, Avtozma, Tyenne:** 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	**Actemra, Avtozma, Tofidence, Tyenne:** 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* **Actemra, Avtozma, Tyenne:** 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
	GCA	**Actemra, Avtozma, Tofidence, Tyenne:** IV: 6 mg/kg every 4 weeks in combination with a tapering course of glucocorticoids **Actemra, Avtozma, Tyenne:** SC: 162 mg SC every week (every other week may be given based on clinical considerations)	IV: 6 mg/kg every 4 weeks SC: 162 mg every week
Tocilizumab (Actemra) and biosimilars (Avtozma, Tyenne)	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 tocilizumab may be administered. The	IV: 800 mg/infusion, up to 4 doses

	Indication	Dosing Regimen	Maximum Dose
		interval between consecutive doses should be at least 8 hours.	
Tocilizumab (Actemra)	SSc-ILD	162 mg SC once weekly	SC: 162 mg every week

VI. Product Availability

Drug Name	Availability
Tocilizumab (Actemra)	• 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
Tocilizumab-anoh (Avtozma)	• Single-dose 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
Tocilizumab-bavi (Tofidence)	• Single-dose vial: 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL
Tocilizumab-aazg (Tyenne)	• 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

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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
J3590, C9399	Subcutaneous tocilizumab (unclassified drugs or biologicals)
Q5133	Injection, tocilizumab-bavi (tofidence), biosimilar, 1 mg
Q5135	Injection, tocilizumab-aazg (tyenne), biosimilar, 1 mg
Q5156	Injection, tocilizumab-anoh (avtozma), biosimilar, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2021 annual review: added combination of bDMARDs under Section III; updated CDAI table with ">" to prevent overlap in classification of severity; references reviewed and updated. RT4: added criteria for new FDA indication, SSc-ILD.	02.23.21	05.21
SSc-ILD: added rheumatologist prescriber option per specialist feedback and added baseline FVC/DLCO requirements; RT4: added information regarding Actemra EUA for COVID-19 hospitalized patients.	06.30.21	08.21
Per August SDC and prior clinical guidance, for RA removed redirection to alternative bDMARDs; for Xeljanz redirection requirements added bypass for members with cardiovascular risk and qualified redirection to apply only for member that has not responded or is intolerant to one or more TNF blockers.	08.25.21	11.21
2Q 2022 annual review: for pJIA, removed redirections to Enbrel and Xeljanz per February SDC; RT4: added newly FDA-approved dosing for intravenous Actemra for GCA; reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated.	05.02.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.13.22	
2Q 2023 annual review: RT4: revised criteria for COVID-19 emergency authorized use to FDA-approved indication; removed Appendix K since Actemra does not have EUA and is approved for COVID-19; updated off-label dosing in Appendix B; references reviewed and updated.	01.03.23	05.23
RT4: added newly approved biosimilar Tofidence to pJIA, RA, sJIA criteria and added "request is for Actemra" for indications not approved for Tofidence use; for pJIA for Tofidence requests, added redirection to preferred agents Actemra, adalimumab product, and Xeljanz; for RA for Tofidence requests, added redirection to preferred agents Actemra, adalimumab product, Kevzara, and Xeljanz/Xeljanz XR or Olumiant; added Tofidence dosing to section V; updated	10.05.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Appendix B with relevant therapeutic alternatives; added Tofidence to section III.B; removed HCPCS code Q0249 as code only applies to Actemra EUA use.		
Per December SDC, added adalimumab-adbm to listed examples of preferred adalimumab products; for RA removed redirection to Kevzara and Olumiant.	12.06.23	02.24
Added HCPCS code [Q5133].	02.22.24	
2Q 2024 annual review: for Castleman's disease, added member has either unicentric disease with HIV-negative and HHV-8-negative or multicentric disease as supported by NCCN compendium; for CRS, added "Carvykti™" to list of CAR T cell examples; added Bimzelx, Zymfentra, Omvoh, Wezlana, Sotyktu, and Velsipity to section III.B; references reviewed and updated. RT4: added newly approved biosimilar Tyenne to RA, GCA, pJIA, and sJIA criteria.	03.25.24	05.24
Per June SDC: for RA and pJIA, added Simlandi to listed examples of preferred adalimumab products. Per SDC: for RA and pJIA, added unbranded adalimumab-aaty to listed examples of preferred adalimumab products.	07.23.24	08.24
RT4: for COVID-19 and GCA, added Tofidence to criteria; for section V, added Tofidence dosing for GCA; added HCPCS code [Q5135] for Tyenne.	08.13.24	
Per SDC: for GCA, removed criteria for failure of "≥ 3 consecutive month trial" of a systemic corticosteroid and "in conjunction with methotrexate or azathioprine"; for pJIA: removed criteria for minimum cJADAS-10 score ≥ 8.5 for documentation of high disease activity and "baseline 10-joint clinical juvenile arthritis disease activity score" in initial criteria; removed criteria for "member is responding positively to therapy as evidenced by a decrease in cJADAS-10 from baseline" in continued therapy; for Appendix I, added pJIA disease activity information per 2019 ACR guidelines.	01.13.25	02.25
2Q 2025 annual review: for sJIA, added redirection to NSAID as an option per clinical practice guidelines and competitor analysis; RT4: added newly approved biosimilar Avtozma to criteria; for CRS, revised criteria from "member has developed refractory CRS related to blinatumomab therapy" to "used as supportive care in severe CRS related to blinatumomab therapy" and added criteria "used as prophylaxis to reduce the risk of CRS when administering teclistamab-cqyv" per NCCN compendium; updated section III.B with Spevigo and biosimilar verbiage; references reviewed and updated. RT4: for Tyenne, added newly approved CRS and COVID-19 indications to criteria.	03.17.25	05.25
RT4: for Avtozma, added newly approved CRS indication to criteria; RT4: for Actemra, updated indication for COVID-19 to include	08.14.25	11.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
pediatric extension; for CRS, GCA, sJIA, and Castleman's disease, added redirection from biosimilars to preferred agent Actemra; for GCA, pJIA, RA, and sJIA, added bypass of conventional therapies if a member has failed a biologic agent to clarify intention of not stepping back from biologic agent to conventional therapy; added HCPCS code [Q5156] for Avtozma. Extended initial approval duration to 12 months for chronic condition indications		

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.