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Subject: Tocilizumab Products (Actemra and Tyenne Injections, and Actemra, Avtozma, Tofidence, and Tyenne Infusions)

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DESCRIPTION:

Tocilizumab (Actemra) is a monoclonal antibody that binds to and ultimately blocks soluble and membrane-bound interleukin-6 (IL-6). Interleukin-6 is a proinflammatory cytokine that affects the function of neutrophils, T-cells, B-cells, monocytes, and osteoclasts and is over-expressed in the synovial tissue in patients with rheumatoid arthritis (RA). Additionally, IL-6 has been linked to other inflammatory conditions including systemic juvenile idiopathic arthritis (SJIA) and polyarticular juvenile idiopathic arthritis (PJIA). Tocilizumab was initially approved by the US Food and Drug Administration (FDA) in January 2010 to reduce the signs and symptoms of moderate to severe RA in adults who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonists. The indication was revised in October 2012 to persons with an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs). In 2011, tocilizumab was approved alone or in combination with methotrexate for the treatment of active SJIA in children 2 years of age or older and in April 2013 tocilizumab was granted approval for the treatment of active PJIA in children 2 years of age or older. In May 2017, subcutaneous tocilizumab was FDA-approved for the treatment of giant cell arteritis (GCA) in adult patients in combination with a tapering course of glucocorticoids. It is the first FDA-approved treatment for this disease. In February 2022, the GCA indication was expanded to include the use of IV tocilizumab. The subcutaneous formulation of tocilizumab was first approved in October 2013 for RA. In May 2018, the subcutaneous formulation was approved for the treatment of PJIA. In September 2018, the subcutaneous formulation was approved for the treatment of SJIA. In March 2021, the subcutaneous formulation was approved for the treatment of systemic sclerosis-associated interstitial lung disease (SSc-ILD) for slowing the rate of decline in pulmonary function in adult patients. The subcutaneous formulation is now FDA-approved for the treatment of RA, PJIA, SJIA, SSc-ILD, and GCA. In August 2017, coinciding with approval of the first chimeric antigen receptor (CAR) T-cell therapy tisagenlecleucel (Kymriah), IV tocilizumab was FDA-approved for the treatment of CAR T-cell-induced severe or life-threatening cytokine release syndrome (CRS) in patients 2 years of age and older. Tocilizumab was granted orphan drug designation by the FDA for the treatment of CAR T cell-induced CRS early in the same month. Actemra also received orphan designation (but not an FDA-approved indication) for the treatment of systemic

sclerosis in 2013.

In 2018 the National Comprehensive Cancer Network (NCCN) began publishing its guideline Management of Immunotherapy-Related-Toxicities. Tocilizumab is recommended (category 2A) for additional disease modifying antirheumatic therapy for management of moderate or severe immunotherapy-related inflammatory arthritis if no improvement after holding immunotherapy and treating with oral corticosteroids or if unable to taper corticosteroids, additional disease modifying antirheumatic therapy for polymyalgia rheumatica if unable to taper prednisone or no improvement in symptoms, and additional therapy for management of immunotherapy-related giant cell arteritis (urgent referral to rheumatology even in mild cases. NCCN also includes recommendation for the use of IV tocilizumab for cytokine release syndrome (CRS) or neurotoxicity related to blinatumomab or CAR T-cell therapy. Tocilizumab is also recommended for acute graft-versus-host disease (GVHD) and Castleman's Disease. In June 2021, the IV use of Actemra was granted an Emergency Use Authorization (EUA) by the FDA 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). In December 2022, IV Actemra was granted FDA-approval for the treatment of hospitalized adult patients with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. In August 2025, the FDA approved an expansion of the COVID-19 indication to include pediatric patients aged 2 years and older. The EUA was coincidently revoked as it was no longer necessary based on the current FDA approval.

In September 2023, the FDA approved the first biosimilar to IV Actemra, tocilizumab-bavi (Tofidence). Tofidence is approved for the treatment of moderately to severely active RA, PJIA, and SJIA. The FDA approval of Tofidence was based on a comprehensive analytical, non-clinical and clinical data package submitted by Biogen to the FDA in September 2022. In March 2024, the FDA approved the second biosimilar to IV Actemra, tocilizumab-aazg (Tyenne). Tyenne is also available as a subcutaneous formulation which launched in July 2024 after the IV formulation. Tyenne SC is the first FDA-approved biosimilar for SC Actemra. In January 2025, the FDA approved the third biosimilar to IV Actemra, tocilizumab-anoh (Avtozma).

RHEUMATOID DISORDERS

Rheumatoid arthritis (RA)

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that primarily affects the joints but can also damage extra-articular organs. The main goal of therapy is to achieve remission, but additional goals include decreased disease activity, prevention of systemic complications, and improved physical functioning. The choice of therapy depends on several factors, including the severity of disease activity when therapy is initiated and the response of the patient to prior therapeutic interventions. American College of Rheumatology (ACR) guidelines list the following guiding principles in the treatment of RA:

- RA requires early evaluation, diagnosis, and management
- Treatment decisions should follow a shared decision-making process
- Treatment decisions should be reevaluated within a minimum of 3 months based on efficacy and tolerability of the disease-modifying antirheumatic drug(s) (DMARDs) chosen
- Recommendations are limited to DMARDs approved by the US FDA for treatment of RA:
    - Conventional synthetic DMARDs (csDMARDs): hydroxychloroquine, sulfasalazine, methotrexate (MTX), leflunomide
    - Biologic DMARDs (bDMARDs): Tumor necrosis factor (TNF) inhibitors (e.g., etanercept, adalimumab, infliximab, golimumab, certolizumab pegol), T cell costimulatory inhibitor (e.g., abatacept), Interleukin (IL)-6 receptor inhibitors (e.g., tocilizumab, sarilumab), anti-CD20 antibody* (e.g., rituximab)

*Recommendations referring to bDMARDs exclude rituximab unless patients have had an inadequate response to TNF inhibitors (in order to be consistent with FDA approval) or have a history of lymphoproliferative disorder for which rituximab is an approved therapy

  - Targeted synthetic DMARDs (tsDMARDs): Janus kinase (JAK) inhibitors (e.g., tofacitinib, baricitinib, upadacitinib)

- Triple therapy refers to hydroxychloroquine, sulfasalazine, and either methotrexate or leflunomide
- Biosimilars are considered equivalent to FDA-approved originator bDMARDs
- Treat-to-target refers to a systematic approach involving frequent monitoring of disease activity using validated instruments and modifications of treatment to minimize disease activity with the goal of reaching a predefined target (low disease activity or remission)

ACR guidelines (2021) are broken down by previous treatment and disease activity:

- DMARD-naïve patients with moderate-to-high disease activity initial treatment:
  - MTX monotherapy is strongly recommended over hydroxychloroquine, sulfasalazine, bDMARDs monotherapy, tsDMARD monotherapy, or combination of MTX plus a non-TNF bDMARD or tsDMARD
  - MTX monotherapy is conditionally recommended over leflunomide, dual or triple csDMARD therapy, or combination MTX plus a TNF inhibitor
- DMARD-naïve patients with low disease activity initial treatment
  - Hydroxychloroquine is conditionally recommended over other csDMARDs
  - Sulfasalazine is conditionally recommended over MTX
  - MTX is conditionally recommended over leflunomide
- Initial therapy in csDMARD-treated patients, but MTX naïve, with moderate-to high disease activity:
  - MTX monotherapy is conditionally recommended over combination MTX and a bDMARD or tsDMARD
- Treatment modifications in patients treated with DMARDs who are not at target:
  - Addition of a bDMARD or tsDMARD is conditionally recommended over triple therapy for patients taking maximally tolerated doses of MTX who are not at target
  - Switching to a bDMARD or tsDMARD of a different class is conditionally recommended over switching to a bDMARD or tsDMARD belonging to the same class for patients taking a bDMARD or tsDMARD who are not at target.

The European Alliance of Associations for Rheumatology (EULAR) guidelines for RA (2022 update) also recommend a treat-to-target approach in therapy. MTX is recommended as first line therapy and should be initiated as soon as the diagnosis of RA is made. If MTX is not clinically appropriate, then an alternative csDMARD should be used as part of the (first) treatment strategy. If initial csDMARD therapy does not produce adequate improvement after 3 months, another csDMARD may be added or switched to as long as poor prognosis factors are absent. In the presence of poor prognosis factors, a bDMARD or JAK inhibitor should be added to csDMARD therapy. If treatment failure occurs with the initial bDMARD or JAK inhibitor, another bDMARD or JAK inhibitor should be considered. If a TNF- or IL-6 receptor inhibitor therapy was initially failed, patients may receive an agent with another mode of action or a second TNF- or IL-6 receptor inhibitor.

Initial dosing of MTX for RA should optimally be 15 mg once weekly, with the dose increased as tolerated and as needed to control signs and symptoms. A fast dose escalation of 5 mg/month to 25-30 mg/week has been associated with higher efficacy, but toxicity with this dosing regimen is a limiting factor. In the presence of sufficient folic acid supplementation, the MTX dose can be rapidly escalated to 25 mg once weekly. The MTX target dose is 25 mg weekly, or the highest tolerable dose.

Polyarticular Juvenile Idiopathic Arthritis (PJIA)

Juvenile idiopathic arthritis (JIA) is arthritis that begins before the 16th birthday and persists for at least 6 weeks with other known conditions excluded. Polyarticular juvenile idiopathic arthritis (PJIA) is a subset of JIA. The ACR defines PJIA as arthritis in more than 4 joints during their disease course and excludes systemic JIA. Treatment goals are aimed at achieving clinically inactive disease and to prevent long-term morbidities, including growth disturbances, joint contractures and destruction, functional limitations, and blindness or visual impairment from chronic uveitis.

The American College of Rheumatology guidelines (2019) (ACR)/Arthritis Foundation recommend the following treatment approach for PJIA:

- Nonsteroidal anti-inflammatory drugs (NSAIDs) are conditionally recommended as adjunct therapy
- Disease modifying antirheumatic drug (DMARD) therapy:
    - Methotrexate (MTX) is conditionally recommended over leflunomide and sulfasalazine
    - Subcutaneous MTX is conditionally recommended over oral MTX
- Intraarticular glucocorticoids are conditionally recommended as adjunct therapy and conditionally recommended for bridging only in patients with moderate to high disease activity
- Strongly recommend against chronic low-dose glucocorticoid use, irrespective of disease activity and/or risk factors
- Strongly recommend combination use of a DMARD and infliximab
- Initial therapy for all patients:
    - DMARD is strongly recommended over NSAID monotherapy
    - MTX monotherapy is conditionally recommended over triple DMARD therapy
    - DMARD is conditionally recommended over a biologic
    - Initial biologic therapy may be considered for patients with risk factors and involvement of high-risk joints (e.g., cervical spine, wrist, hip), high disease activity, and/or those judged by their physician to be at high risk of disabling joint damage
- Subsequent therapy:
    - Low disease activity:
        - Escalating therapy (e.g., intraarticular glucocorticoid injections, optimization of DMARD dose, trial of MTX if not already done, and adding or changing biologic agent)
    - Moderate to high disease activity:
        - Add a biologic to original DMARD over changing to a second DMARD or changing to triple DMARD therapy
        - Switch to a non- tumor necrosis factor (TNF) biologic if currently treated with first TNF-inhibitor ± DMARD over switching to another TNF-inhibitor (unless the patient had good initial response to first TNF-inhibitor)
        - TNF-inhibitor, abatacept, or tocilizumab (depending on prior biologics received) over rituximab after trial of second biologic

Systemic Juvenile Idiopathic Arthritis (SJIA)

Systemic juvenile idiopathic arthritis (SJIA) is a subset of juvenile idiopathic arthritis (JIA). SJIA is distinct from all other categories of JIA due to fever, rash, and visceral involvement. Disease pathogenesis and cytokine involvement in SJIA are different than other JIA categories. SJIA is now considered to be the same disease as adult onset Still's disease (AOSD) under the umbrella term Still's disease, recognizing

that the previous distinction of the two disorders by age of onset (before or after 16 years of age) was mainly artificial.

SJIA has been defined as:

- Onset of symptoms occurring before the age of 16 years
- Arthritis in greater than or equal to 1 joint for at least 6 weeks' duration
- Fever of at least 2 weeks' duration (documented to be daily ["quotidian"] for at least 3 days)
- Accompanied by one or more of the following:
    - Evanescent (nonfixed) erythematous rash
    - Generalized lymphadenopathy (lymph node enlargement)
    - Hepatomegaly and/or splenomegaly
    - Serositis (pericarditis, pleuritis, and/or peritonitis)

The European Alliance of Associations for Rheumatology (EULAR)/Paediatric Rheumatology European Society (PReS) 2024 guidelines strongly recommend that the presence of arthritis not be mandatory for the diagnosis of Still's disease. Arthralgia is commonly present at disease onset, but arthritis often presents later with a median delay of 1 month. Requiring arthritis to make the diagnosis leads to unnecessary treatment delays. Instead, a patient with fever for at least 7 days, rash, arthralgia/myalgia, and elevated inflammatory markers should be sufficient to facilitate rapid diagnosis and initiate early treatment.

Macrophage activation syndrome (MAS), a secondary hemophagocytic syndrome, is a life-threatening complication requiring urgent recognition and treatment. MAS presents with fever, high ferritin levels, cytopenia, elevated liver enzyme levels, low fibrinogen levels, and high triglyceride levels. As it may occur at any point during the disease course, including during treatment, careful monitoring is necessary for children with or without MAS at presentation. MAS is the most frequent complication, occurring in 15% to 20% of patients. Goals of therapy for SJIA include control of active inflammation and symptoms, and the prevention of a number of disease and/or treatment related morbidities, such as growth disturbances, joint damage, and functional limitations.

An interleukin (IL)-1 or IL-6 inhibitor should be used as initial treatment for SJIA. The IL-1/IL-6 should be initiated as early as possible when the diagnosis of SJIA is established or during a flare, irrespective of disease severity. Early initiation of an IL-1 or IL-6 inhibitor has been shown to have favorable outcomes, limit or avoid corticosteroid use, limit a chronic persistent disease course, and also does not interfere with the diagnostic work-up at onset. EULAR/PReS strongly recommends their use based on their efficacy to control all aspects of the disease, including both systemic and joint manifestations.

Glucocorticoids can be used short-term in patients with severe symptoms, risk of MAS, and/or severe pericarditis. High dose glucocorticoids are the mainstay of treatment in patients with MAS, being added on to biologic therapy. For some patients with MAS, biologic therapy combined with glucocorticoids and calcineurin inhibitors may be necessary to control the disease. Glucocorticoids may also be helpful at disease onset to control systemic and joint manifestations until IL-1 or IL-6 inhibitors can be started.

Non-steroidal anti-inflammatory drugs (NSAIDs) are sometimes used as a brief trial for initial treatment for SJIA without MAS. Studies suggest that a small proportion of patients will respond to NSAIDs alone, however many prescribers prefer that the use of NSAIDs be avoided altogether for SJIA. NSAIDs are typically only used to assist in controlling symptoms, such as fever or arthralgia. Conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) have historically been used, but evidence supporting their efficacy is scarce. Methotrexate is sometimes used in patients with arthritis.

OTHER DISORDERS

Giant Cell Arteritis (GCA)

Giant cell arteritis (GCA) is a blood vessel disease that predominantly affects medium to large arteries in individuals older than 50 years of age, causing clinical manifestations in both cranial and extracranial locations. The cranial phenotype is characterized by headache, jaw claudication, and visual disturbance or loss. The extracranial phenotype is characterized by musculoskeletal involvement with symptoms associated with polymyalgia rheumatica, such as pain, stiffness, and limited range of motion around the shoulders, neck, and hips. Treatment should begin as soon as the diagnosis is made to prevent loss of vision or blindness.

The American College of Rheumatology/Vasculitis Foundation guidelines (2021) recommend high-dose systemic glucocorticoids as the mainstay of therapy for GCA. The guidelines provide the following recommendations for the management of GCA:

- Patients with newly diagnosed active GCA with visual symptoms/loss or critical cranial ischemia:
    - High dose IV pulse corticosteroids followed by high dose oral corticosteroids with or without a non-corticosteroid immunosuppressive agent (i.e., methotrexate or tocilizumab)
    - Taper oral corticosteroids in patients that achieve remission
    - Consider adding on or changing non-corticosteroid immunosuppressive agent in patients that have not achieved remission
- Patients with newly diagnosed active GCA without visual symptoms/loss or critical cranial ischemia:
    - High dose oral corticosteroids with or without a non-corticosteroid immunosuppressive agent (i.e., methotrexate or tocilizumab)
    - Taper oral corticosteroids in patients that achieve remission
    - Consider adding on or changing non-corticosteroid immunosuppressive agent in patients that have not achieved remission

Cytokine Release Syndrome

Cytokine release syndrome (CRS) is a non-antigen specific toxicity that occurs due to a high-level immune activation, secondary to receiving cancer immunotherapy and CAR T-cell therapy. Large numbers of lymphocytes and/or myeloid cells release inflammatory cytokines when they become activated. Symptoms and severity depend on the level of immune activation and the inducing agent. Fever is the hallmark symptom of CRS, and potential life-threatening complications can include cardiac dysfunction, respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation. CRS severity is graded on a scale of 1 to 5, with 5 being death. The American Hematology Association recommends symptomatic treatment for grade 1 CRS and notes immunosuppressive therapy may be used to treat grade 2 with extensive co-morbidities or advanced age. Grades 3 and 4 should be treated with immunosuppression in an attempt to suppress the inflammatory cascade and prevent irreversible organ damage. Tocilizumab is recommended as the first line immunosuppressive therapy with or without corticosteroids.

Systemic Sclerosis (Scleroderma)-Associated Interstitial Lung Disease (ILD)

Systemic sclerosis (SSc) is a connective tissue disease (CTD) that affects numerous organ systems, including skin, blood vessels, heart, lungs, kidneys, gastrointestinal, and musculoskeletal. Pulmonary disease is the leading cause of death in patients with systemic sclerosis, and ILD is a common manifestation that tends to occur early in the course of systemic sclerosis.

SSc-associated ILD (SSc-ILD) is diagnosed when there is radiographic evidence of diffuse parenchymal lung disease in patients with systemic sclerosis. ILD is defined as pulmonary fibrosis seen on high-resolution computed tomography (HRCT) or chest radiography, most pronounced in the basilar portions of the lungs.(54) All patients with suspected SSc-ILD should undergo HRCT of the chest at initial evaluation. HRCT is preferred over pulmonary function tests (PFTs) since patients with ILD can have

normal PFTs or have difficulty performing them due to cough or microstomia. HRCT is also preferred over chest radiography due to its low sensitivity, which limits its use as a screening test for ILD.

The American College of Rheumatology (ACR) and American College of Chest Physicians (CHEST) guidelines (2023) recommend the following treatment options for SSc-ILD:

- Note: Treatments are listed in order based on a hierarchy established by the voting panel, but it is noted that the decision on which first-line therapy to use is dependent on specific situations and patient factors
- Preferred therapies: mycophenolate, tocilizumab, rituximab
- Additional options: cyclophosphamide, nintedanib, azathioprine

The American Thoracic Society (ATS) guidelines (2023) state the following for the treatment of SSc-ILD:

- Recommends the use of [strong in favor]: mycophenolate
- Suggests the use of [conditional in favor]: cyclophosphamide, rituximab, tocilizumab, nintedanib, nintedanib plus mycophenolate

POSITION STATEMENT:

Drug Waste Reduction: Additional medical necessity criteria for dose optimization may apply to intravenous tocilizumab products depending on the requested dose and member's benefit. Refer to Medical Coverage Guideline Drug Waste Reduction, 09-J5000-54.

Site of Care: If intravenous tocilizumab (Actemra), tocilizumab-aazg (Tyenne), tocilizumab-anoh (Avtozma), or tocilizumab-bavi (Tofidence) is administered in a hospital-affiliated outpatient setting, additional requirements may apply depending on the member's benefit. Refer to 09-J3000-46: Site of Care Policy for Select Specialty Medications.

Comparative Effectiveness

The Food and Drug Administration has deemed the subcutaneously-administered drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) of the subcutaneous formulation of tocilizumab in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary. This statement does not apply to the intravenous (IV) formulations of tocilizumab (Actemra), tocilizumab-aazg (Tyenne), tocilizumab-anoh (Avtozma), or tocilizumab-bavi (Tofidence).

NOTE: The list of self-administered products with prerequisites for certain indications can be found at Preferred Agents and Drug List.

SUBCUTANEOUS TYENNE (PHARMACY BENEFIT)

Initiation of subcutaneous tocilizumab-aazg (Tyenne) [i.e., the preferred subcutaneous tocilizumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "5"):

1. **ONE** of the following ("a", "b", or "c"):
    a. The member has been treated with subcutaneous tocilizumab-aazg (Tyenne) (starting on samples is not approvable) within the past 90 days
    b. The prescriber states the member has been treated with subcutaneous tocilizumab-aazg (Tyenne) (starting on samples is not approvable) within the past 90 days **AND** is at risk if therapy is changed
    c. **BOTH** of the following ('i" and "ii"):

i. Subcutaneous tocilizumab-aazg (Tyenne) will be used for the treatment of an indication listed in Table 1, and **ALL** of the indication-specific criteria are met

ii. **EITHER** of the following if the member has an FDA-approved indication ("I" or "II")

I. The member's age is within FDA labeling for the requested indication for subcutaneous tocilizumab-aazg (Tyenne)

II. The prescriber has provided information in support of using subcutaneous tocilizumab-aazg (Tyenne) for the member's age for the requested indication

2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA; pulmonologist, radiologist, pathologist, rheumatologist for SSc-ILD) or has consulted with a specialist in the area of the member's diagnosis
3. Member does **NOT** have any FDA labeled contraindications to subcutaneous tocilizumab-aazg (Tyenne)
4. Member will **NOT** be using subcutaneous tocilizumab-aazg (Tyenne) in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
5. **ANY** of the following ("a". "b", "c", or "d"):
   a. The dosage does not exceed 162 mg SQ every week
      - QL: 162 mg/0.9 mL pen - 4 pens (3.6 mL)/28 days
      - QL: 162 mg/0.9 mL syringe - 4 syringes (3.6 mL)/28 days
   b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
      i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
      ii. **ALL** of the following ("1", "2", and "3"):
         1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication
         2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)
         3. **EITHER** of the following ("a" or "b"):
            a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit
            b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)
   c. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit

ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

d. The member does **NOT** have an FDA labeled indication NOR a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):

i. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

Approval duration: 12 months

Table 1

Indications and Specific Criteria	
Indication	**Specific Criteria**
Moderately to severely active rheumatoid arthritis (RA)	**BOTH** of the following: 1. **ONE** of the following: a. The member has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) after at least a 3-month duration of therapy **OR** b. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA after at least a 3-month duration of therapy **OR** c. The member has an intolerance or hypersensitivity to **ONE** conventional agent (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** d. The member has an FDA labeled contraindication to **ALL** conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** e. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of RA

	AND 2. **ANY** of the following: a. The member has tried and had an inadequate response to at least **ONE** preferred adalimumab product for at least a 3-month trial **OR** b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to at least **ONE** preferred adalimumab product **OR** c. The member has an FDA labeled contraindication to **ALL** preferred adalimumab products **OR** d. **ALL** preferred adalimumab products are not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication **The preferred adalimumab products are:** • Adalimumab-aaty • Adalimumab-adaz • Hadlima (adalimumab-bwwd) • Humira (adalimumab) • Simlandi (adalimumab-ryvk)
Giant cell arteritis (GCA)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** systemic corticosteroid (e.g., prednisone, methylprednisolone) used in the treatment of GCA after at least a 7-day duration of therapy **OR** 2. The member has an intolerance or hypersensitivity to **ONE** systemic corticosteroid used in the treatment of GCA **OR** 3. The member has an FDA labeled contraindication to **ALL** systemic corticosteroids used in the treatment of GCA **OR** 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of GCA
Active systemic juvenile idiopathic arthritis (SJIA)	Diagnosis only
Moderately to severely active polyarticular	**BOTH** of the following: 1. **ONE** of the following:

juvenile idiopathic arthritis (PJIA)	a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA for at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PJIA **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PJIA **OR** d. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PJIA **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to at least **ONE** preferred adalimumab product after at least a 3-month trial **OR** b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to at least **ONE** preferred adalimumab product **OR** c. The member has an FDA labeled contraindication to **ALL** preferred adalimumab products **OR** d. **ALL** preferred adalimumab products are not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication: **The preferred adalimumab products are:** • Adalimumab-aaty • Adalimumab-adaz • Hadlima (adalimumab-bwwd) • Humira (adalimumab) • Simlandi (adalimumab-ryvk)
Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD)	The patient's diagnosis has been confirmed on high-resolution computed tomography (HRCT) or chest radiography scans

Other indications	The member has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a

Continuation of subcutaneous tocilizumab-aazg (Tyenne) [i.e., the preferred subcutaneous tocilizumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "6"):

1. An authorization or reauthorization for subcutaneous tocilizumab-aazg (Tyenne) has been previously approved by Florida Blue [Note: members not previously approved for the requested agent will require initial evaluation review]
2. Member has had clinical benefit with subcutaneous tocilizumab-aazg (Tyenne) therapy
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA; pulmonologist, radiologist, pathologist, rheumatologist for SSc-ILD) or has consulted with a specialist in the area of the member's diagnosis
4. Member does **NOT** have any FDA labeled contraindications to subcutaneous tocilizumab-aazg (Tyenne)
5. Member will **NOT** be using subcutaneous tocilizumab-aazg (Tyenne) in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. **ANY** of the following ("a". "b", "c", or "d"):
    a. The dosage does not exceed 162 mg SQ every week
        - QL: 162 mg/0.9 mL pen - 4 pens (3.6 mL)/28 days
        - QL: 162 mg/0.9 mL syringe - 4 syringes (3.6 mL)/28 days
    b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
        i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
        ii. **ALL** of the following ("1", "2", and "3"):
            1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication
            2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)
            3. **EITHER** of the following ("a" or "b"):
                a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit
                b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

c. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

   i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit

   ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

d. The member does **NOT** have an FDA labeled indication **NOR** a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):

   i. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

   ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

Approval duration: 12 months

SUBCUTANEOUS ACTEMRA (PHARMACY BENEFIT)

Initiation of subcutaneous tocilizumab (Actemra) [i.e., the non-preferred subcutaneous tocilizumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "6"):

1. **BOTH** of the following ("a" and "b"):

   a. Subcutaneous tocilizumab (Actemra) will be used for the treatment of an indication listed in Table 2, and **ALL** of the indication-specific criteria are met

   b. **EITHER** of the following if the member has an FDA-approved indication ("i" or "ii"):

      i. The member's age is within FDA labeling for the requested indication for subcutaneous tocilizumab (Actemra)

      ii. The prescriber has provided information in support of using subcutaneous tocilizumab (Actemra) for the member's age for the requested indication

2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA; pulmonologist, radiologist, pathologist, rheumatologist for SSc-ILD) or has consulted with a specialist in the area of the member's diagnosis

3. Member does **NOT** have any FDA labeled contraindications to subcutaneous tocilizumab (Actemra)

4. Member will **NOT** be using subcutaneous tocilizumab (Actemra) in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

5. If subcutaneous tocilizumab (Actemra) is requested for a diagnosis of systemic sclerosis associated interstitial lung disease, the request is for the Actemra syringe (NOTE: Actemra ACTpen is not approvable for SSc-ILD)

6. **ANY** of the following ("a". "b", "c", or "d"):

   a. The dosage does not exceed 162 mg SQ every week

- QL: 162 mg/0.9 mL pen - 4 pens (3.6 mL)/28 days
- QL: 162 mg/0.9 mL syringe - 4 syringes (3.6 mL)/28 days

b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

   i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

   ii. **ALL** of the following ("1", "2", and "3"):

      1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication

      2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)

      3. **EITHER** of the following ("a" or "b"):

         a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit

         b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

c. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

   i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit

   ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

d. The member does **NOT** have an FDA labeled indication **NOR** a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):

   i. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

   ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

Approval duration: 12 months

Table 2

Indications and Specific Criteria	
Indication	**Specific Criteria**

Moderately to severely active rheumatoid arthritis (RA)	**BOTH** of the following: 1. **ONE** of the following: a. The member has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) after at least a 3-month duration of therapy **OR** b. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA after at least a 3-month duration of therapy **OR** c. The member has an intolerance or hypersensitivity to **ONE** conventional agent (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** d. The member has an FDA labeled contraindication to **ALL** conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** e. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of RA **AND** 2. **ANY** of the following (submitted medical records/chart notes are required for confirmation): a. The member has tried and had an inadequate response to **BOTH** Tyenne (tocilizumab-aazg) after at least a 3-month trial **AND** at least **ONE** preferred adalimumab product after at least a 3-month trial **OR** b. The member has tried and had an inadequate response to Tyenne (tocilizumab-aazg) after at least a 3-month trial **OR** at least **ONE** of the preferred adalimumab product after at least a 3-month duration of therapy, **AND** an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to Tyenne (tocilizumab-aazg) **OR** at least **ONE** preferred adalimumab product **OR** c. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **BOTH** Tyenne (tocilizumab-aazg) **AND** at least **ONE** preferred adalimumab product **OR** d. The member has an FDA labeled contraindication to **BOTH** Tyenne (tocilizumab-aazg) **AND ALL** preferred adalimumab products

	OR e. **BOTH** Tyenne (tocilizumab-aazg) **AND ALL** preferred adalimumab products are not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication **The preferred adalimumab products are:** • Adalimumab-aaty • Adalimumab-adaz • Hadlima (adalimumab-bwwd) • Humira (adalimumab) • Simlandi (adalimumab-ryvk)
Giant cell arteritis (GCA)	**BOTH** of the following: 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** systemic corticosteroid (e.g., prednisone, methylprednisolone) used in the treatment of GCA for at least a 7-day duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** systemic corticosteroid used in the treatment of GCA **OR** c. The member has an FDA labeled contraindication to **ALL** systemic corticosteroids used in the treatment of GCA **OR** d. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of GCA **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to Tyenne (tocilizumab-aazg) after at least a 3-month trial **OR** b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to Tyenne (tocilizumab-aazg) **OR** c. The member has an FDA labeled contraindication to Tyenne (tocilizumab-aazg) **OR**

	d. Tyenne (tocilizumab-aazg) is not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication
Active systemic juvenile idiopathic arthritis (SJIA)	**ANY** of the following: 1. The member has tried and had an inadequate response to Tyenne (tocilizumab-aazg) after at least a 3-month trial **OR** 2. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to Tyenne (tocilizumab-aazg) **OR** 3. The member has an FDA labeled contraindication to Tyenne (tocilizumab-aazg) **OR** 4. Tyenne (tocilizumab-aazg) is not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication
Moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA)	**BOTH** of the following: 1. **ONE** of the following: a. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA for at least a 3-month duration of therapy **OR** b. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PJIA **OR** c. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PJIA **OR** d. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PJIA **AND** 2. **ANY** of the following (submitted medical records/chart notes are required for confirmation): a. The member has tried and had an inadequate response to **BOTH** Tyenne (tocilizumab-aazg) after at least a 3-month trial **AND** at least **ONE** preferred adalimumab products after at least a 3-month trial **OR**

	b. The member has tried and had an inadequate response to Tyenne (tocilizumab-aazg) after at least a 3-month trial **OR** at least **ONE** of the preferred adalimumab product after at least a 3-month duration of therapy, **AND** an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to Tyenne (tocilizumab-aazg) **OR** at least **ONE** preferred adalimumab product **OR** c. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **BOTH** Tyenne (tocilizumab-aazg) **AND** at least **ONE** preferred adalimumab product **OR** d. The member has an FDA labeled contraindication to **BOTH** Tyenne (tocilizumab-aazg) **AND ALL** preferred adalimumab products **OR** e. **BOTH** Tyenne (tocilizumab-aazg) **AND ALL** preferred adalimumab products are not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication **The preferred adalimumab products are:** • Adalimumab-aaty • Adalimumab-adaz • Hadlima (adalimumab-bwwd) • Humira (adalimumab) • Simlandi (adalimumab-ryvk)
Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD)	**BOTH** of the following: 1. The patient's diagnosis has been confirmed on high-resolution computed tomography (HRCT) or chest radiography scans **AND** 2. **ANY** of the following: a. The member has tried and had an inadequate response to Tyenne (tocilizumab-aazg) after at least a 3-month trial **OR** b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to Tyenne (tocilizumab-aazg) **OR** c. The member has an FDA labeled contraindication to Tyenne (tocilizumab-aazg) **OR**

	d. Tyenne (tocilizumab-aazg) is not clinically appropriate for the member, **AND** the prescriber has provided a complete list of previously tried products for the requested indication

Continuation of subcutaneous tocilizumab (Actemra) [i.e., the non-preferred subcutaneous tocilizumab product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "8"):

1. An authorization or reauthorization for subcutaneous tocilizumab (Actemra) has been previously approved by Florida Blue [Note: members not previously approved for the requested agent will require initial evaluation review]
2. Member has had clinical benefit with subcutaneous tocilizumab (Actemra) therapy
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA; pulmonologist, radiologist, pathologist, rheumatologist for SSc-ILD) or has consulted with a specialist in the area of the member's diagnosis
4. Member does **NOT** have any FDA labeled contraindications to subcutaneous tocilizumab (Actemra)
5. Member will **NOT** be using subcutaneous tocilizumab (Actemra) in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
6. The member meets the following prerequisite biologic immunomodulator agent requirements depending on the indication for use:
    a. RA – see bullets 2a to 2d in Table 2 (submitted medical records/chart notes are required for confirmation
    b. GCA - see bullets 2a to 2d in Table 2
    c. SJIA – see bullets 1 to 4 in Table 2
    d. PJIA - see bullets 2a to 2d in Table 2 (submitted medical records/chart notes are required for confirmation)
    e. SSc-ILD - see bullets 2a to 2d in Table 2
7. If subcutaneous tocilizumab (Actemra) is requested for a diagnosis of systemic sclerosis associated interstitial lung disease, the request is for the Actemra syringe (NOTE: Actemra ACTpen is not approvable for SSc-ILD)
8. **ANY** of the following ("a". "b", "c", or "d"):
    a. The dosage does not exceed 162 mg SQ every week
        i. QL: 162 mg/0.9 mL pen - 4 pens (3.6 mL)/28 days
        ii. QL: 162 mg/0.9 mL syringe - 4 syringes (3.6 mL)/28 days
    b. The member has an FDA labeled indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):
        i. The requested quantity (dose) does **NOT** exceed the maximum FDA labeled dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
        ii. **ALL** of the following ("1", "2", and "3"):

1. The requested quantity (dose) exceeds the FDA maximum labeled dose for the requested indication
2. The member has tried and had an inadequate response to at least a 3-month trial of the maximum FDA labeled dose for the requested indication (medical records required)
3. **EITHER** of the following ("a" or "b"):
    a. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit
    b. The requested quantity (dose) exceeds the maximum FDA labeled dose **AND** the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)
    b. The member has a compendia supported indication for the requested agent, **AND EITHER** of the following ("i" or "ii"):

i. The requested quantity (dose) does **NOT** exceed the maximum compendia supported dose for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength/and or package size that does not exceed the program quantity limit

ii. The requested quantity (dose) exceeds the maximum compendia supported dose for the requested indication, **AND** there is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

c. The member does **NOT** have an FDA labeled indication **NOR** a compendia supported indication for the requested agent, **AND BOTH** of the following ("i" and "ii"):

i. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

ii. There is support for therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

Approval duration: 12 months

INTRAVENOUS TOCILIZUMAB PRODUCTS - ACTEMRA, AVTOZMA, TOFIDENCE, AND TYENNE (MEDICAL BENEFIT)

Initiation of intravenous (IV) tocilizumab-aazg (Tyenne) [i.e., the preferred tocilizumab IV product] **meets the definition of medical necessity** when **ALL** of the following are met ("1" and "4"):

1. Tocilizumab-aazg (Tyenne) will be used for the treatment of an indication listed in Table 3 and **ALL** of the indication-specific and maximum-allowable dose criteria are met
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA) or has consulted with a specialist in the area of the member's diagnosis
3. Member does **NOT** have any FDA labeled contraindications to tocilizumab-aazg (Tyenne)
4. Member will **NOT** be using tocilizumab-aazg (Tyenne) in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast);

Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

Approval duration: 12 months (except for CRS, COVID-19, and immune checkpoint inhibitor-related inflammatory arthritis which are approved for 1 month, and acute GVHD which is approved for 6 months)

Initiation of intravenous (IV) tocilizumab (Actemra), IV tocilizumab-anoh (Avtozma), or IV tocilizumab-bavi (Tofidence) [i.e., the non-preferred IV tocilizumab products] **meets the definition of medical necessity** when **ALL** of the following are met ("1" and "5"):

1. The requested IV tocilizumab product will be used for the treatment of an indication listed in Table 3 and **ALL** of the indication-specific and maximum-allowable dose criteria are met
2. The member has previously tried IV tocilizumab-aazg (Tyenne) and was either unable to tolerate and/or had an inadequate response – documentation of the intolerance or inadequate response must be submitted
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA) or has consulted with a specialist in the area of the member's diagnosis
4. Member does **NOT** have any FDA labeled contraindications to the requested IV tocilizumab product
5. Member will **NOT** be using the requested IV tocilizumab product in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

Approval duration: 12 months (except for CRS, COVID-19, and immune checkpoint inhibitor-related inflammatory arthritis which are approved for 1 month, and acute GVHD which is approved for 6 months)

Table 3

Indications and Specific Criteria		
Indication	**Specific Criteria**	**Maximum Allowable Dose***
Moderately to severely active rheumatoid arthritis (RA)	**ONE** of the following: 1. The member has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) after at least a 3-month duration of therapy **OR** 2. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA after at least a 3-month duration of therapy **OR** 3. The member has an intolerance or hypersensitivity to **ONE** conventional agent (i.e., methotrexate, hydroxychloroquine,	8 mg/kg (maximum of 800 mg) every 4 weeks

	leflunomide, sulfasalazine) used in the treatment of RA **OR** 4. The member has an FDA labeled contraindication to **ALL** conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA **OR** 5. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of RA	
Giant cell arteritis (GCA)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** systemic corticosteroid (e.g., prednisone, methylprednisolone) used in the treatment of GCA for at least a 7 -day duration of therapy **OR** 2. The member has an intolerance or hypersensitivity to **ONE** systemic corticosteroid used in the treatment of GCA **OR** 3. The member has an FDA labeled contraindication to **ALL** systemic corticosteroids used in the treatment of GCA **OR** 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of GCA	6 mg/kg (maximum of 600 mg) every 4 weeks
Cytokine release syndrome (CRS)	When **BOTH** of the following are met ("1" and "2"): 1. **EITHER** of the following ("a" or "b"): a. Member is experiencing CRS symptoms (e.g., fever, vascular leak, hypotension, pulmonary edema, coagulopathy, organ failure) **OR** b. Tocilizumab is being ordered proactively in anticipation of possible CRS	Less than 30 kg: • 12 mg/kg • No more than 4 total doses given at least 8 hours apart 30 kg or above: • 8 mg/kg (not to exceed 800 mg)

	AND 2. The member has received **EITHER** of the following in the previous 30 days, **OR** will be receiving **EITHER** of the following in the next 30 days (if tocilizumab is being ordered proactively): a. CAR T-cell therapy b. Bispecific T-cell engaging (BiTE) monoclonal antibody therapy [examples include - blinatumomab (Blincyto), elranatamab (Elrexfio), epcoritamab (Epkinly), glofitamab (Columvi), mosunetuzumab (Lunsumio), talquetamab (Talvey), tarlatamab (Imdelltra), tebentafusp (Kimmtrak), and teclistamab (Tecvayli)]	• No more than 4 total doses given at least 8 hours apart
Immune checkpoint inhibitor-related adverse effects/toxicity	When **ALL** of the following are met ("1", "2", and "3"): 1. Member has been receiving treatment with an immune checkpoint inhibitor (e.g., ipilimumab, nivolumab, pembrolizumab, atezolizumab, avelumab, darvalumab) **AND** 2. Member has **ANY** of the following immunotherapy-related adverse effects: a. Grade 2 elevated alanine transaminase/aspartate transaminase (ALT/AST) if liver enzymes suggest worsening or no improvement after 3 to 7 days of prednisone b. Grade 3 or 4 elevated ALT/AST if no improvement after 1 to 2 days of prednisone/methylprednisolone if refractory to mycophenolate mofetil or tacrolimus c. Grade 2 elevated alkaline phosphatase (predominant) with or without bilirubin/AST/ALT elevations if alkaline phosphatase worsens or does not improve within 3 days after initiating corticosteroids d. Grade 3 or 4 elevated alkaline phosphatase (predominant) with or without bilirubin/AST/ALT elevations if no improvement after 1 to 2 days of prednisone/methylprednisolone AND ursodiol	4 mg/kg X 1 dose. May repeated one additional 4 mg/kg dose if the member does not have adequate improvement in symptoms.

	e. Hemophagocytic lymphohistiocytosis (HLH)-like syndrome if no response to corticosteroids after 5 days f. Moderate or severe inflammatory arthritis if unable to taper corticosteroids after 1 week g. Giant cell arteritis (urgent referral to rheumatology even in mild cases)Moderate (G2) pneumonitis if no improvement after 48 to 72 hours of corticosteroids h. Severe (G3-4) pneumonitis if no improvement after 48 hours of IV methylprednisolone	
Kaposi-sarcoma associated herpesvirus (KSHV)-Associated Inflammatory Cytokine Syndrome (KICS)	Member has refractory/progressive disease	Less than 30 kg: • 12 mg/kg • No more than 4 total doses given at least 8 hours apart 30 kg or above: • 8 mg/kg (not to exceed 800 mg) • No more than 4 total doses given at least 8 hours apart
Active systemic juvenile idiopathic arthritis (SJIA)	Diagnosis only	Less than 30 kg: • 12 mg/kg every 2 weeks 30 kg or above: • 8 mg/k every 2 weeks
Moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA after at least a 3-month duration of therapy **OR** 2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PJIA	Less than 30 kg: • 10 mg/kg every 4 weeks 30 kg or above: • 8 mg/k every 4 weeks

	OR 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PJIA **OR** 4. The member's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PJIA	
Unicentric Castleman's disease (CD)	When **ALL** of the following are met ("1", "2", "3", and "4"): 1. Used as monotherapy for treatment of CD **AND** 2. Member's disease is relapsed or refractory **OR** progressive and unresectable **AND** 3. Member is HIV-negative **AND** 4. Member is human herpesvirus-8-negative	12 mg/kg every 2 weeks
Multicentric Castleman's disease (CD)	When **ALL** of the following are met ("1", "2, and 3"): 1. Used as monotherapy for treatment of CD **AND** 2. Members disease is relapsed or refractory **AND** 3. Member has had an inadequate therapeutic response to at least **TWO** prior treatments	12 mg/kg every 2 weeks
Neuromyelitis optica spectrum disorder (NMOSD)	When **BOTH** of the following are met ("1" and "2"): 1. Member has a history of at least 1 relapse in the previous year **AND** 2. Tocilizumab will not be used concurrently with an alternative biologic agent for the treatment of NMOSD (e.g., eculizumab, inebilizumab, rituximab, satralizumab)	8 mg/kg (maximum of 800 mg) every 4 weeks
Acute graft-versus-host disease (GVHD)	**ALL** of the following ("1" to "3"): 1. The member has previously received an allogeneic hematopoietic stem cell transplantation (HSCT)	8 mg/kg (maximum of 800 mg) every 2 weeks

	AND 2. Tocilizumab will be used as additional therapy in conjunction with systemic corticosteroids **AND** 3. The member has steroid-refractory disease	
Coronavirus disease 2019 (COVID-19) treatment	**ALL** of the following ("1" to "4"): 1. Member is hospitalized **AND** 2. Member is 2 years of age or older **AND** 3. Member is receiving systemic corticosteroids **AND** 4. Member requires supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)	Less than 30 kg: • 12 mg/kg X 1 dose 30 kg or above: • 8 mg/kg X 1 dose (maximum of 800 mg) May repeat one additional dose at least 8 hours after the first dose if clinical signs or symptoms worsen or do not improve.
Orphan Indications (non-FDA approved)		
Systemic sclerosis	When **BOTH** of the following are met ("1"and "2"): 1. Member has severe disease with diffuse skin involvement, interstitial lung disease, myocarditis, and/or inflammatory myopathy or arthritis **AND** 2. Member is refractory to systemic immunosuppressive therapy with methotrexate, mycophenolate, or cyclophosphamide, **OR** has intolerable adverse effects with or a contraindication to immunosuppressive therapy	12 mg/kg every 2 weeks
Other indications	The member has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a	Maximum dose supported by the FDA labeled indication or maximum dose supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a
*The maximum allowable dose can be exceeded if - (1) the dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested		

indication, **OR** (2) the prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Continuation of intravenous (IV) tocilizumab (Actemra), IV tocilizumab-aazg (Tyenne), IV tocilizumab-anoh (Avtozma), or IV tocilizumab-bavi (Tofidence) **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "7"):

1. An authorization or reauthorization for IV tocilizumab, IV tocilizumab-aazg, IV tocilizumab-anoh (Avtozma), or IV tocilizumab-bavi has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of a condition in Table 3 (except for CRS, acute GVHD, COVID-19, and immune checkpoint inhibitor-related inflammatory arthritis – see initiation criteria), **OR** the member previously met **ALL** indication-specific initiation criteria.
2. For IV tocilizumab (Actemra), IV tocilizumab-anoh (Avtozma), and IV tocilizumab-bavi (Tofidence) [i.e., the non-preferred IV tocilizumab products] **ONLY** - The member has previously tried IV tocilizumab-aazg (Tyenne) and was either unable to tolerate and/or had an inadequate response – documentation of the intolerance or inadequate response must be submitted
3. The prescriber is a specialist in the area of the member's diagnosis (e.g., rheumatologist for JIA, PsA, RA) or has consulted with a specialist in the area of the member's diagnosis
4. Member does **NOT** have any FDA labeled contraindications to the requested IV tocilizumab product
5. Member has had clinical benefit with the requested IV tocilizumab product
6. Member will **NOT** be using the requested IV tocilizumab product in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Rinvoq/Rinvoq LQ (upadacitinib), and Xeljanz/Xeljanz XR (tofacitinib)]; Otezla/Otezla XR (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
7. **EITHER** of the following ("a" or "b"):
    a. The dosage does not exceed the following based on the specific indication and member weight:
        - RA and NMOSD: 8 mg/kg IV (max of 800 mg) every 4 weeks
        - GCA: 6 mg/kg IV (max of 600 mg) every 4 weeks
        - SJIA/SJRA:
            - Less than 30 kg: 12 mg/kg IV every 2 weeks
            - 30 kg or above: 8 mg/kg IV every 2 weeks
        - JIA:
            - Less than 30 kg: 10 mg/kg IV every 4 weeks
            - 30 kg or above: 8 mg/kg IV every 4 weeks
        - Castleman's Disease and systemic sclerosis: 12 mg/kg IV every 2 weeks

    b. The dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication, **OR** the prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy of clinical trials, phase III studies, guidelines required)

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved:

Actemra

Tocilizumab is indicated for the treatment of the following conditions:

- Rheumatoid arthritis (RA) in adult patients with moderately to severely active disease who have had an inadequate response to one or more DMARDs (both the IV and SQ routes are FDA-approved)
- Giant cell arteritis (GCA) in adult patients (both the IV and SQ routes are FDA-approved)
- Systemic sclerosis-associated interstitial lung disease (SSc-ILD) for slowing the rate of decline in pulmonary function in adult patients (only the SQ route is FDA-approved)
- Polyarticular juvenile idiopathic arthritis (PJIA) in persons 2 years of age or older with active disease (both the IV and SQ routes are FDA-approved)
- Systemic juvenile idiopathic arthritis (SJIA) in persons 2 years of age or older with active disease (both the IV and SQ routes are FDA-approved)
- Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older (only the IV route is FDA-approved)
- Coronavirus disease 2019 (COVID-19) in hospitalized adult and pediatric patients aged 2 years and older who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO (only the IV route is FDA-approved)

For the treatment of RA, GCA, PJIA, and SJIA, tocilizumab can be administered as an IV infusion drip over 1 hour or a subcutaneous injection. When administered intravenously, it should not be administered as an IV bolus or push. Initially, the subcutaneous injection should be administered under the guidance of a healthcare practitioner. After proper training, a member may self-inject tocilizumab or the member's caregiver may administer tocilizumab if the healthcare practitioner determines that it is appropriate.

For RA, GCA, SSc-ILD, PJIA and SJIA, therapy should not be initiated in persons with an absolute neutrophil count (ANC) less than 2000 per mm^3, platelet count less than 100,000 mm^3, or an ALT/AST greater than 1.5 times the upper limit of normal (ULN). For COVID-19, therapy should not be initiated in persons with an ANC less than 1000 per mm^3, platelet count below 50,000 mm^3, or ALT or AST greater than 10 times ULN. The recommended dosage, based on indication, is identified in Table 4.

Table 4

FDA-approved indications and dosing		
Indication	**Dose**	
GCA	IV infusion	6 mg/kg (up to a max of 600 mg) every 4 weeks in combination with a tapering course of glucocorticoids. Actemra can be used alone following discontinuation of glucocorticoids.
	SQ injection	162 mg given once every week in combination with a tapering course of glucocorticoids. Every other week dosing may be prescribed based on clinical considerations. Actemra can be used alone following discontinuation of glucocorticoids. When transitioning from intravenous therapy to subcutaneous administration, administer the first subcutaneous dose instead of the next scheduled intravenous dose.

SSc-ILD	SQ injection	162 mg given once every week. Subcutaneous administration with the prefilled ACTPen autoinjector has not been studied in SSc-ILD.	
RA	IV infusion	4 mg/kg every 4 weeks initially, followed by an increase to 8 mg/kg every 4 weeks based on clinical response. The dose should not exceed 800 mg per infusion.	
	SQ injection	Less than 100 kg	162 mg SQ every other week, followed by an increase to weekly based on clinical response
		At or above 100 kg	162 mg SQ every week
COVID-19	IV infusion	Patients less than 30 kg weight – 12 mg/kg. Patients at or above 30 kg weight - 8 mg/kg (not to exceed 800 mg). If clinical signs or symptoms worsen or do not improve after the first dose, one additional infusion may be administered at least 8 hours after the initial infusion.	
CRS	IV infusion	Less than 30 kg	12 mg/kg IV X 1 dose. If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses may be administered. The interval between consecutive doses should be at least 8 hours.
		30 kg or more	8 mg/kg (not to exceed 800 mg) IV X 1 dose. If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses may be administered. The interval between consecutive doses should be at least 8 hours.
PJIA	IV infusion	Less than 30 kg	10 mg/kg IV every 4 weeks
		At or above 30 kg	8 mg/kg IV every 4 weeks
	SQ injection	Less than 30 kg	162 mg once every 3 weeks
		At or above 30 kg	162 mg once every 2 weeks
SJIA	IV infusion	Less than 30 kg	12 mg/kg IV every 2 weeks
		At or above 30 kg	8 mg/kg IV every 2 weeks
	SQ injection	Less than 30 kg	162 mg once every 2 weeks
		At or above 30 kg	162 mg once every week
GCA, giant cell arteritis; RA, rheumatoid arthritis; CRS, cytokine release syndrome; COVID-19, Coronavirus disease 2019; PJIA, polyarticular juvenile idiopathic arthritis; SJIA, systemic juvenile idiopathic arthritis			

Dosage Adjustments: Table 5 reviews recommended dose modifications for laboratory abnormalities associated with treatment of RA, SSc-ILD, and GCA. Dose reduction of tocilizumab has not been studied in SJIA and PJIA populations. Dose interruptions are recommended for liver enzyme abnormalities, low neutrophil counts, and low platelet counts in persons with SJIA and PJIA at levels similar to what is outline for persons with RA.

Table 5

Dose Modifications		
Laboratory Abnormality	**Lab Value**	**Recommendation**
Liver enzymes	Greater than 1 to 3x ULN	Dose modify concomitant DMARDs or immunomodulatory agents if appropriate.

		For persistent increases in this range • IV: reduce tocilizumab dose to 4 mg/kg or interrupt tocilizumab until ALT or AST have normalized • SQ: reduce injection frequency to every other week or hold dosing until ALT/AST have normalized. Resume every other week and increase frequency to every week as clinically appropriate
	Greater than 3 to 5x ULN (confirmed by repeat testing)	Interrupt tocilizumab dosing until less than 3x ULN and follow recommendations above for greater than 1 to 3x ULN. For persistent increases greater than 3x ULN, discontinue tocilizumab.
	Greater than 5x ULN	Discontinue tocilizumab.
Low ANC	Greater than 1000	Maintain dose.
	500-1000	Interrupt tocilizumab dosing. When ANC greater than 1000 cells per mm3: • IV: resume tocilizumab at 4 mg/kg and increase to 8 mg/kg as clinically appropriate • SQ: resume at every other week and increase frequency to every week as clinically appropriate
	Less than 500	Discontinue tocilizumab.
Low platelet count		Interrupt tocilizumab dosing. When platelet count is greater than 100,000 cells per mm3: • IV: resume tocilizumab at 4 mg/ kg and increase to 8 mg/kg as clinically appropriate • SQ: resume at every other week and increase frequency to every week as clinically appropriate.
	Less than 50,000	Discontinue tocilizumab.
ULN, upper limit of normal; DMARD, disease modifying anti-rheumatic drug; ANC, absolute neutrophil count		

Avtozma

Tocilizumab- anoh is indicated for the treatment of the following conditions:

- Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
- Adult patients with giant cell arteritis (GCA)
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis

- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis
- Adults and pediatric patients with 2 years of age and older with chimeric antigen recept (CAR) T cell-induced severe or life-threatening cytokine release syndrome
- Hospitalized adult patients with coronavirus disease 2019 (COVID-19) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)

Refer to Actemra for dosing recommendations and dosing modifications.

Tofidence

Tocilizumab-bavi is indicated for the treatment of the following conditions:

- Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
- Adult patients with giant cell arteritis
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis
- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis
- Hospitalized adult patients with coronavirus disease 2019 (COVID-19) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)

Refer to Actemra for dosing recommendations and dosing modifications.

Tyenne

Tocilizumab-aazg is indicated for the treatment of the following conditions:

- Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs) [IV and SQ]
- Adult patients with giant cell arteritis (GCA) [IV and SQ]
- Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis [IV and SQ]
- Patients 2 years of age and older with active systemic juvenile idiopathic arthritis [IV and SQ]
- Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older (only the IV route is FDA-approved)
- Coronavirus disease 2019 (COVID-19) in hospitalized adult patients who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) (only the IV route is FDA-approved)

Refer to Actemra for dosing recommendations and dosing modifications.

Drug Availability:

Tocilizumab (Actemra) is supplied in the following strengths:

IV Formulation

- 80 mg/4 mL as a single-use vial
- 200 mg/10 mL as a single-use vial
- 400 mg/20 mL as a single-use vial

SQ Formulation

- 162 mg single-use ACTPen autoinjector
- 162 mg single-use prefilled glass syringe

Must be refrigerated at 36°F to 46°F (2ºC to 8ºC). Do not freeze. Protect the vials, syringes, and autoinjectors from light by storage in the original package until time of use, and keep syringes and autoinjectors dry. Once removed from the refrigerator, the prefilled syringe and autoinjector can be stored up to 2 weeks at or below 86°F (30°C). The prefilled syringe and autoinjector must always be kept in the carton.

Tocilizumab-anoh (Avtozma) is supplied in the following strengths:

- 80 mg/4 mL as a single-use vial
- 200 mg/10 mL as a single-use vial
- 400 mg/20 mL as a single-use vial

Must be refrigerated at 36°F to 46°F (2ºC to 8ºC). Do not freeze. Protect the vials from light by storage in the original package until time of use.

Tocilizumab-bavi (Tofidence) is supplied in the following strengths:

- 80 mg/4 mL as a single-use vial
- 200 mg/10 mL as a single-use vial
- 400 mg/20 mL as a single-use vial

Must be refrigerated at 36°F to 46°F (2ºC to 8ºC). Do not freeze. Protect the vials from light by storage in the original package until time of use.

Tocilizumab-aazg (Tyenne) is supplied in the following strengths:

IV Formulation

- 80 mg/4 mL as a single-use vial
- 200 mg/10 mL as a single-use vial
- 400 mg/20 mL as a single-use vial

SQ Formulation

- 162 mg single-use autoinjector
- 162 mg single-use prefilled syringe

Must be refrigerated at 36°F to 46°F (2ºC to 8ºC). Do not freeze. Protect the vials, syringes, and autoinjectors from light by storage in the original package until time of use and keep syringes and autoinjectors dry. A single prefilled syringe (or autoinjector) may be stored at room temperature at or below 77°F (25°C) for a single period of up to 14 days.

PRECAUTIONS:

Boxed Warning

- WARNING: RISK OF SERIOUS INFECTIONS

Patients treated with tocilizumab products are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

If a serious infection develops, interrupt Actemra/Tofidence until the infection is controlled.

Reported infections include:

- Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients, except those with COVID-19, should be tested for latent tuberculosis before Actemra/Tofidence use and during therapy. Treatment for latent infection should be initiated prior to Actemra/Tofidence use.
- Invasive fungal infections, including candidiasis, aspergillosis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
- Bacterial, viral and other infections due to opportunistic pathogens.

The risks and benefits of treatment with Actemra/Tofidence should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Actemra/Tofidence, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Contraindication

- Do not administer to persons with a history of hypersensitivity to tocilizumab products.

Precautions/Warnings

- **Gastrointestinal perforation:** use with caution in persons who may be at an increased risk.
- **Hepatotoxicity**: monitor patients for signs and symptoms of hepatic injury. Modify or discontinue tocilizumab if abnormal liver tests persist or worsen or if clinical signs and symptoms of liver disease develop.
- **Laboratory monitoring:** recommended due to potential consequences of treatment-related changes in neutrophils, platelets, lipids, and liver function tests.
- **Live vaccines:** do not administer with tocilizumab.

BILLING/CODING INFORMATION:

HCPCS Coding:

J3262	Injection, tocilizumab, 1 mg [for intravenous Actemra]
J3590	Unclassified biologics [for subcutaneous Actemra ONLY]
M0233	Intravenous infusion, tocilizumab-aazg, for hospitalized adult patients with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ecmo) only, includes infusion and post administration monitoring, first dose
M0234	Intravenous infusion, tocilizumab-aazg, for hospitalized adult patients with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ecmo) only, includes infusion and post administration monitoring, second dose
M0237	Intravenous infusion, tocilizumab-anoh, for hospitalized adult patients with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal

	membrane oxygenation (ecmo) only, includes infusion and post administration monitoring, first dose
M0238	Intravenous infusion, tocilizumab-anoh, for hospitalized adult patients with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ecmo) only, includes infusion and post administration monitoring, second dose
M0249	Intravenous infusion, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) only, includes infusion and post administration monitoring, first dose
M0250	Intravenous infusion, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) only, includes infusion and post administration monitoring, second dose
Q0237	Injection, tocilizumab-anoh, for hospitalized adult patients with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ecmo) only, 1 mg
Q0238	Injection, tocilizumab-aazg, for hospitalized adult patients with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ecmo) only, 1 mg
Q0249	Injection, tocilizumab, for hospitalized adults and pediatric patients (2 years of age and older) with covid-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) only, 1 mg
Q5133	Injection, tocilizumab-bavi (Tofidence), biosimilar, 1 mg
Q5135	Injection, tocilizumab-aazg (Tyenne), biosimilar, 1 mg [for intravenous and subcutaneous Tyenne]
Q5156	Injection, tocilizumab-anoh (Avtozma), biosimilar, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity for J3262, Q5133, Q5135 (Tyenne IV only: NCDs 65219-0590-04, 65219-0592-10, and 65219-0594-20), and Q5156:

B10.89	Other human herpesvirus infection
D47.Z2	Castleman disease
D89.810	Acute graft-versus-host disease
D89.812	Acute on chronic graft-versus-host disease
D89.832	Cytokine release syndrome, grade 2
D89.833	Cytokine release syndrome, grade 3
D89.834	Cytokine release syndrome, grade 4
D89.839	Cytokine release syndrome, grade unspecified
G36.0	Neuromyelitis optica [Devic]
G92.00	Immune effector cell-associated neurotoxicity syndrome, grade unspecified
G92.01	Immune effector cell-associated neurotoxicity syndrome, grade 1
G92.02	Immune effector cell-associated neurotoxicity syndrome, grade 2
G92.03	Immune effector cell-associated neurotoxicity syndrome, grade 3
G92.04	Immune effector cell-associated neurotoxicity syndrome, grade 4
M05.00 – M05.09	Felty's syndrome
M05.10 – M05.19	Rheumatoid lung disease with rheumatoid arthritis
M05.20 – M05.29	Rheumatoid vasculitis with rheumatoid arthritis

M05.30 – M05.39	Rheumatoid heart disease with rheumatoid arthritis
M05.40 – M05.49	Rheumatoid myopathy with rheumatoid arthritis
M05.50 – M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis
M05.60 – M05.69	Rheumatoid arthritis with involvement of other organs and systems
M05.70 – M05.7A	Rheumatoid arthritis with rheumatoid factor without organ or systems involvement
M05.80 – M05.8A	Other rheumatoid arthritis with rheumatoid factor
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M05.A	Abnormal rheumatoid factor and anti-citrullinated protein antibody with rheumatoid arthritis
M06.00 – M06.0A	Rheumatoid arthritis without rheumatoid factor
M06.20 – M06.29	Rheumatoid bursitis
M06.30 – M06.39	Rheumatoid nodule
M06.80 – M06.8A	Other specified rheumatoid arthritis
M06.9	Rheumatoid arthritis, unspecified
M08.09	Unspecified juvenile rheumatoid, multiple sites
M08.20 – M08.2A	Juvenile rheumatoid arthritis with systemic onset
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.89	Other juvenile arthritis, multiple sites
M31.5	Giant cell arteritis with polymyalgia rheumatica
M31.6	Other giant cell arteritis
M34.0 – M34.9	Systemic sclerosis [scleroderma]
R59.0 – R59.9	Enlarged lymph nodes
T45.AX5A	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, initial encounter
T45.AX5D	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, subsequent encounter
T45.AX5S	Adverse effect of immune checkpoint inhibitors and immunostimulant drugs, sequela
T80.82XA	Complication of immune effector cellular therapy, initial encounter
T80.82XS	Complication of immune effector cellular therapy, subsequent encounter
U07.1	COVID-19 [only valid for HCPCS codes M0233, M0234, M0237, M0238, M0249, M0250, Q0237, Q0238, and Q0249]

ICD-10 Diagnosis Codes That Support Medical Necessity for J3590 (for Actemra SC ONLY) and Q5135 (Tyenne SC only: NCDs 65219-0584-01 and 65219-0586-04):

M05.00 – M05.09	Felty's syndrome
M05.10 – M05.19	Rheumatoid lung disease with rheumatoid arthritis
M05.20 – M05.29	Rheumatoid vasculitis with rheumatoid arthritis
M05.30 – M05.39	Rheumatoid heart disease with rheumatoid arthritis
M05.40 – M05.49	Rheumatoid myopathy with rheumatoid arthritis
M05.50 – M05.59	Rheumatoid polyneuropathy with rheumatoid arthritis
M05.60 – M05.69	Rheumatoid arthritis with involvement of other organs and systems
M05.70 – M05.7A	Rheumatoid arthritis with rheumatoid factor without organ or systems involvement
M05.80 – M05.8A	Other rheumatoid arthritis with rheumatoid factor
M05.9	Rheumatoid arthritis with rheumatoid factor, unspecified
M05.A	Abnormal rheumatoid factor and anti-citrullinated protein antibody with rheumatoid arthritis
M06.00 – M06.0A	Rheumatoid arthritis without rheumatoid factor
M06.20 – M06.29	Rheumatoid bursitis
M06.30 – M06.39	Rheumatoid nodule
M06.80 – M06.8A	Other specified rheumatoid arthritis

M06.9	Rheumatoid arthritis, unspecified
M08.09	Unspecified juvenile rheumatoid, multiple sites
M08.20 – M08.2A	Juvenile rheumatoid arthritis with systemic onset
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.89	Other juvenile arthritis, multiple sites
M31.5	Giant cell arteritis with polymyalgia rheumatica
M31.6	Other giant cell arteritis
M34.81	Systemic sclerosis with lung involvement

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date. The Site of Care Policy for Select Specialty Medications does not apply to Medicare Advantage members.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

B cells: lymphocytes that play a large role in the humoral immune response (as opposed to the cell-mediated immune response, which is governed by T cells). The principal functions of B cells are to make antibodies against antigens, perform the role of antigen-presenting cells (APCs) and eventually develop into memory B cells after activation by antigen interaction. B cells are an essential component of the adaptive immune system.

Cytokines: any of a number of substances that are secreted by specific cells of the immune system which carry signals locally between cells, and thus have an effect on other cells.

DMARDs: An acronym for disease-modifying antirheumatic drugs. These are drugs that modify the rheumatic disease processes, and slow or inhibit structural damage to cartilage and bone. These drugs are unlike symptomatic treatments such as NSAIDs that do not alter disease progression. DMARDs can be further subcategorized. With the release of biologic agents (e.g., anti-TNF drugs), DMARDs were divided into either: (1) conventional, traditional, synthetic, or non-biological DMARDs; or as (2) biological DMARDs. However, with the release of newer targeted non-biologic drugs and biosimilars, DMARDs are now best categorized as: (1) conventional synthetic DMARDs (csDMARD) (e.g., MTX, sulfasalazine), (2) targeted synthetic DMARDs (tsDMARD) (e.g., tofacitinib, apremilast), and (3) biological DMARDs (bDMARD), which can be either a biosimilar DMARD (bsDMARD) or biological originator DMARD (boDMARD).

Fibroblast: a type of cell that synthesizes the extracellular matrix and collagen, the structural framework (stroma) for animal tissues, and plays a critical role in wound healing.

Interleukin-6 (IL-6): a protein that in humans is encoded by the IL6 gene. It acts as both a pro-inflammatory and anti-inflammatory cytokine. It is secreted by T cells and macrophages to stimulate immune response to trauma, especially burns or other tissue damage leading to inflammation.

Lymphocyte: a type of white blood cell in the vertebrate immune system.

Macrophages: white blood cells within tissues, produced by the division of monocytes.

Monocyte: a type of white blood cell, part of the human body's immune system.

Rheumatoid arthritis: usually strikes between ages 20 and 50. Inflammation begins in a joint, usually those of the fingers and hands, resulting in pain, swelling, redness, and eventually joint deformity. It is considered an autoimmune disease, which can affect the entire body, causing fatigue, weight loss, weakness, fever, and loss of appetite. It affects each person differently, with symptoms ranging from mild to debilitating. In many cases, it is difficult to control. In about one in six cases, rheumatoid arthritis becomes severely debilitating and can shorten the life of the person affected.

T cells or T lymphocytes: belong to a group of white blood cells known as lymphocytes and play a central role in cell-mediated immunity.

RELATED GUIDELINES:

Abatacept (Orencia), 09-J0000-67
Adalimumab (Humira), 09-J0000-46
Anakinra (Kineret), 09-J0000-45
Baricitinib (Olumiant), 09-J3000-10
Certolizumab Pegol (Cimzia), 09-J0000-77
Etanercept (Enbrel), 09-J0000-38
Golimumab (Simponi, Simponi Aria), 09-J1000-11
Infliximab Products [infliximab (Remicade), infliximab-dyyb (Inflectra), and infliximab-abda (Renflexis)], 09-J0000-39
Sarilumab (Kevzara), 09-J2000-87
Tofacitinib (Xeljanz, Xeljanz XR) Oral Solution, Tablet and Extended-Release Tablet, 09-J1000-86
Upadacitinib (Rinvoq), 09-J3000-51

OTHER:

NOTE: The list of biologic immunomodulator agents not permitted as concomitant therapy can be found at Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.

Table 6: Conventional Synthetic DMARDs

DMARD Generic Name	DMARD Brand Name
Auranofin (oral gold)	Ridaura
Azathioprine	Imuran
Cyclosporine	Neoral, Sandimmune
Hydroxychloroquine	Plaquenil
Leflunomide	Arava
Methotrexate	Rheumatrex, Trexall
Sulfasalazine	Azulfidine, Azulfidine EN-Tabs

Table 7: Grading of Severity of Rheumatoid Arthritis

Severity	Criteria
Mild	Joint pain Inflammation of at least 3 joints No inflammation in tissues other than the joints Usually, a negative result on a rheumatoid factor test

	An elevated erythrocyte sedimentation rate (ESR) or C reactive protein (CRP) level No evidence of bone or cartilage damage on x-rays
Moderate	Between 6 and 20 inflamed joints Usually no inflammation in tissues other than the joints An elevated ESR or CRP levels A positive rheumatoid factor test or anti-cyclic citrullinated peptide (anti-CCP) antibodies Evidence of inflammation but no evidence of bone damage on x-rays
Severe	More than 20 persistently inflamed joints or a rapid loss of functional abilities Elevated ESR or CRP levels Anemia related to chronic illness Low blood albumin level A positive rheumatoid factor test, often with a high level Evidence of bone and cartilage damage on x-ray Inflammation in tissues other than joints

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Committee on 11/12/25.

GUIDELINE UPDATE INFORMATION:

05/15/10	New Medical Coverage Guideline.
01/01/11	Revision to guideline; consisting of updating coding.
07/15/11	Review and revision to guideline; consisting of adding new indication of SJIA, updating dosing, coding and references.
07/15/12	Review and revision to guideline; consisting of reformatting position statement, dosage and administration, precautions and references.
01/15/13	Revision to guideline; consisting of modifying coverage criteria for rheumatoid arthritis.
09/15/13	Review and revision to guideline; consisting of revising description, position statement, dosage administration, and precautions; updating program exceptions and references.
01/01/14	Revision to guideline; consisting of updating position statement and adding new formulation.
04/15/14	Revision to guideline; consisting of revising position statement.
09/15/14	Review and revision to guideline; consisting of updating position statement and references.
09/15/15	Review and revision to guideline; consisting of updating description section, position statement, billing/coding, related guidelines, and references.
11/01/15	Revision: ICD-9 Codes deleted.
09/15/16	Review and revision to guideline consisting of updating description section, position statement, billing/coding, related guidelines, and references.
10/01/16	Revision: ICD-10 code updates.

05/15/17	Revision to guideline consisting of clarifying language in the description section and position statement.
07/15/17	Revision to guideline consisting of updating the position statement, dosage/administration section, coding/billing, and references to include a new FDA-approved indication of giant cell arteritis (GCA).
10/15/17	Review and revision to guideline consisting of updating description, position statement, dosage/administration, coding/billing, definitions, related guidelines, and references.
01/01/18	Revision to guideline consisting of updating the preferred self-administered biologic products according to indication for use. Tofacitinib (Xeljanz, Xeljanz XR) added as prerequisite therapy for rheumatoid arthritis when tocilizumab is used as self-administered subcutaneous therapy.
05/15/18	Revision to guideline consisting of updating the position statement, dosage/administration, and coding/billing.
07/01/18	Revision to guideline consisting of the position statement.
07/15/18	Revision to guideline consisting of updating the description section, position statement, dosage/administration, coding/billing, and references based on FDA approval of SQ administration for PJIA and new NCCN guideline for management of immunotherapy-related toxicities.
10/15/18	Review and revision to guideline consisting of updating the position statement, description, dosage/administration, related guidelines, and references.
10/15/19	Review and revision to guideline consisting of updating the position statement, precautions, and references.
11/11/19	Revision to guideline consisting of adding a reference to the Site of Care Policy for Select Specialty Medications and updating the Program Exceptions.
01/01/20	Revision to guideline consisting of updating the position statement due to changes in preferred and non-preferred products.
07/01/20	Revision to guideline consisting of updating the description and position statement.
01/01/21	Review and revision to guideline consisting of updating the position statement and references.
03/15/21	Revision to guideline consisting of updating Table 1 in the position statement.
08/15/21	Revision to guideline consisting of updating the consisting of updating the description section, position statement, dosage/administration, coding/billing, other section, and references.
10/01/21	Revision: Addition of HCPCS codes M0249, M0250, and Q0249. Addition of ICD-10 code range G92.00 – G92.05.
11/15/21	Revision to guideline consisting of updating the position statement.
01/01/22	Review and revision to guideline consisting of updating the description, position statement, and references.
02/15/22	Update to Table 1 in Position Statement.
03/15/22	Revision to guideline consisting of updating the position statement and other section.
04/15/22	Revision to guideline consisting of updating the description section, position statement, dosage/administration section, and references.
05/15/22	Update to Table 1 in Position Statement.
07/15/22	Update to Table 1 in Position Statement.
09/15/22	Update to Table 1 in Position Statement.
01/01/23	Review and revision to guideline consisting of updating the position statement, other section, and references. New drugs were added to the list of drugs that are not permitted for use in combination.
03/15/23	Revision to guideline consisting of updating the description section, position statement, dosage/administration, precautions, and references based on the FDA approval of IV Actemra for the treatment of certain hospitalized adults with COVID-19.

04/15/23	Revision to guideline consisting of updating the description section, position statement, and references related to SSc-ILD. The conventional agent prerequisites were removed for SSc-ILD.
07/01/23	Revision to guideline consisting of updating the position statement and other section. Amjevita and Hadlima added as Step 1a agents. Humira biosimilar products added to list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.
01/01/24	Review and revision to guideline consisting of updating the description, position statement, dosage/administration, precautions, billing/coding, other section, and references. Added tocilizumab-bavi (Tofidence) IV infusion to guideline, the first biosimilar to Actemra IV. It is covered at parity with IV Actemra with the same indications and criteria. Tofidence is included in the Site of Care Program. For SJIA indication, removed NSAIDs step requirement. Amjevita low concentration [10 mg/0.2 mL, 20 mg/0.4 mL, and 40 mg/0.8 mL concentrations only] clarified as the preferred prerequisite product. Updated the immune checkpoint inhibitor-related adverse effects criteria. Update to Table 1 in Position Statement. New drugs were added to the list of drugs that are not permitted for use in combination.
04/01/24	Revision: Added HCPCS code Q5133.
07/01/24	Revision to guideline consisting of updating the description, position statement, dosage/administration, billing/coding, other section, and references. Added tocilizumab-aazg (Tyenne) IV infusion to guideline, the second biosimilar to Actemra IV. It is covered at parity with IV Actemra and IV Tofidence with the same indications and criteria. Amjevita low-concentration removed as a preferred agent. Rinvoq added as a Step 1b product for PJIA. Removal of latent TB testing requirement. New drugs added to the list of Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.
07/15/24	Revision to guideline consisting of updating the position statement to allow the use of IV tocilizumab for the treatment of CRS related to bispecific T-cell engaging (BiTE) monoclonal antibody therapy.
10/01/24	Revision to guideline consisting of updating the position statement and billing/coding. Updates to Table 1. Simlandi added among the required prerequisite agents for self-administered Actemra for RA and PJIA. Rinvoq LQ added among the required prerequisite agents for self-administered Actemra for PJIA. Added HCPCS code Q5135. New ICD-10 codes.
11/15/24	Revision to guideline consisting of updating the position statement, other section, and billing/coding. HCPCS code Q5135 applies to both IV and SC Tyenne. The applicable ICD-10 code depends on if Tyenne is SC or IV.
01/01/25	Review and revision to guideline consisting of updating the position statement, other section, and references. Adalimumab-aaty and Adalimumab-adaz added among the preferred adalimumab products. Subcutaneous (SC) tocilizumab-aazg (Tyenne) is now the preferred SC tocilizumab product. Tyenne SC added as a step 1a agent for GCA, SJIA, and SSc-ILD, and added as a step 2 agent (stepped through a preferred adalimumab product) for PJIA and RA. Subcutaneous (SC) tocilizumab (Actemra) was moved to step 2 (stepped though Tyenne) for GCA, SJIA, and SSc-ILD, and moved from a step 2 to step 3b for PJIA and RA (stepped though both Tyenne and preferred adalimumab product). Intravenous (IV) tocilizumab-aazg (Tyenne) is now the preferred IV tocilizumab product. Both IV tocilizumab (Actemra) and IV tocilizumab-bavi (Tofidence) are non-preferred and stepped though Tyenne IV for both new starts and continuation of therapy. Update to original Table 1 which is now a link out from the Position Statement. Table titles updated. Revised wording regarding maximum dosage exceptions for Actemra SC and Tyenne SC. New drugs were added to the list of drugs that are not permitted for use in combination.
10/01/25	Revision: Added ICD-10 code M05.A.
01/01/26	Review and revision to guideline consisting of updating the description, position statement, dosage/administration, billing/coding, and references. Avtozma added as a non-preferred IV tocilizumab product (stepped through Tyenne IV), Revised criteria for Immune checkpoint inhibitor-related toxicity per NCCN updates.

04/01/26	Revision: Added HCPCS codes M0233, M0234, M0237, M0238, Q0237, and Q0238.
06/01/26	Revision: Added Drug Waste Reduction statement to the Position Statement.