LOUISIANA BLUE

tocilizumab Products

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Rheumatoid Arthritis

Based on review of available data, the Company may consider the use of both intravenous and subcutaneous tocilizumab (Actemra®)‡, tocilizumab-bavi (Tofidence™)‡, tocilizumab-aazg (Tyenne®)‡, and tocilizumab-anoh (Avtozma®)‡ for the treatment of rheumatoid arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of both intravenous and subcutaneous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of rheumatoid arthritis will be considered when ALL of the following patient selection criteria are met:

Initial

- Patient is 18 years of age or older; AND
- Patient has a diagnosis of moderately to severely active rheumatoid arthritis; AND
- Patient has failed treatment with one or more traditional disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Requested drug is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira®, biosimilars)‡ or etanercept (Enbrel®)‡, or other drugs such as apremilast (Otezla®)‡ or tofacitinib (Xeljanz/XR®)‡; AND
- For tocilizumab (Actemra) and tocilizumab-aazg (Tyenne) subcutaneous requests ONLY (this criterion is NOT applicable to the intravenous version): Patient has failed treatment with adalimumab (Simlandi®, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals], adalimumab-ryvk [manufactured by Quallent Pharmaceuticals])‡ after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals], adalimumab-ryvk [manufactured by Quallent Pharmaceuticals]) will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Patient has a negative tuberculosis (TB) test (e.g., purified protein derivative [PPD], blood test) prior to treatment; AND
- For tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) intravenous requests only: Dose does not exceed 8 milligrams per kilogram every 4 weeks.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- For tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) intravenous requests only: Dose does not exceed 8 milligrams per kilogram every 4 weeks.

Systemic Juvenile Idiopathic Arthritis

Based on review of available data, the Company may consider the use of both intravenous and subcutaneous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of systemic juvenile idiopathic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of both intravenous and subcutaneous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of active systemic juvenile idiopathic arthritis will be considered when ALL of the following patient selection criteria are met:

Initial

- Patient is 2 years of age and older; AND
- Patient has a diagnosis of active systemic juvenile idiopathic arthritis; AND
- Patient has an inadequate clinical response to nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), or other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND

- For intravenous requests for tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma), patient meets ONE of the following:
    - If patient is less than 30 kg, the dose will not exceed 12 milligrams per kilogram every 2 weeks; OR
    - If patient is at or above 30 kg, the dose will not exceed 8 milligrams per kilogram every 2 weeks.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as resolution of fever, reduction in rash or other skin manifestations, normalization of inflammatory markers (e.g., C-reactive protein or erythrocyte sedimentation rate), decreased corticosteroid requirements, reduced joint pain, stiffness, or swelling, diminished fatigue, or enhanced ability to perform daily activities; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- For intravenous requests for tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma), patient meets ONE of the following:
    - If patient is less than 30 kg, the dose will not exceed 12 milligrams per kilogram every 2 weeks; OR
    - If patient is at or above 30 kg, the dose will not exceed 8 milligrams per kilogram every 2 weeks.

Polyarticular Juvenile Idiopathic Arthritis

Based on review of available data, the Company may consider the use of both intravenous and subcutaneous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of active polyarticular juvenile idiopathic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of both intravenous and subcutaneous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of active polyarticular juvenile idiopathic arthritis will be considered when ALL of the following patient selection criteria are met:

Initial

- Patient is 2 years of age and older; AND
- Patient has a diagnosis of active polyarticular juvenile idiopathic arthritis; AND

- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- For tocilizumab (Actemra) and tocilizumab-aazg (Tyenne) subcutaneous requests ONLY (this criterion is NOT applicable to the intravenous version): Patient has failed treatment with adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals], adalimumab-ryvk [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests the use of adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals], adalimumab-ryvk [manufactured by Quallent Pharmaceuticals]) will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested drug is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), or other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- For intravenous requests for tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma), patient meets ONE of the following:
  - If patient is less than 30 kg, the dose will not exceed 10 milligrams per kilogram every 4 weeks; OR
  - If patient is at or above 30 kg, the dose will not exceed 8 milligrams per kilogram every 4 weeks.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as improved range of motion, reduced joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living, reduced corticosteroid dosage, or improvement in inflammatory serum markers; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), OR potent immunosuppressants such as azathioprine and cyclosporine, OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND

- For intravenous requests for tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma), patient meets ONE of the following:
    - If patient is less than 30 kg, the dose will not exceed 10 milligrams per kilogram every 4 weeks; OR
    - If patient is at or above 30 kg, the dose will not exceed 8 milligrams per kilogram every 4 weeks.

Giant Cell Arteritis

Based on review of available data, the Company may consider the use of both intravenous and subcutaneous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of giant cell arteritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of both intravenous and subcutaneous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of giant cell arteritis will be considered when the following patient selection criteria are met:

Initial:

- Patient has a diagnosis of giant cell arteritis; AND
- Patient is 18 years of age or older; AND
- Patient is using requested drug in combination with a tapering course of glucocorticoids; AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- Requested drug is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), or other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has failed treatment with systemic corticosteroid therapy unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- For tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) intravenous requests only: Dosage is 6 milligrams per kilogram every 4 weeks.

Continuation:

- Patient received initial authorization for the requested drug; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as decreased headache, scalp, or jaw pain, reduced fatigue, improved vision, reduced corticosteroid dosage, or improvement in inflammatory serum markers; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Requested drug is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), or other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- For tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) intravenous requests only: Dosage is 6 milligrams per kilogram every 4 weeks.

Cytokine Release Syndrome

Based on review of available data, the Company may consider the use of intravenous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of cytokine release syndrome to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of intravenous tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for the treatment of cytokine release syndrome will be considered when the following patient selection criteria are met:

- Patient is 2 years of age and older; AND
- Patient has a diagnosis of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome. Severe or life-threatening cytokine release syndrome is defined as having either hemodynamic instability despite intravenous fluids and vasopressor support OR worsening respiratory distress, including pulmonary infiltrates, increasing oxygen requirement including high-flow oxygen and/or need for mechanical ventilation OR rapid clinical deterioration; AND
- No more than 4 total doses of tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), or tocilizumab-anoh (Avtozma) (to not exceed 800 mg per infusion) should be administered per event of cytokine release syndrome.

Systemic Sclerosis Associated Interstitial Lung Disease (SSc-ILD)

Based on review of available data, the Company may consider the use of subcutaneous tocilizumab (Actemra) for the treatment of systemic sclerosis associated interstitial lung disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of subcutaneous tocilizumab (Actemra) for the treatment of systemic sclerosis associated interstitial lung disease will be considered when the following patient selection criteria are met:

Initial:

- Patient has a diagnosis of systemic sclerosis associated interstitial lung disease (SSc-ILD) as confirmed by chest high resolution computed tomography (HRCT) WITHOUT contrast; AND
- Patient is experiencing a decline in pulmonary function; AND
- Patient is 18 years of age or older; AND

- Patient has a Forced Vital Capacity (FVC) greater than 55% of the predicted value; AND
  *(Note: This specific patient selection criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has tried and failed (e.g., intolerance or inadequate response) mycophenolate mofetil after at least 6 months of therapy unless there is clinical evidence or patient history that suggests the use of mycophenolate mofetil will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient will not use the requested drug in combination with nintedanib (Ofev®)‡ for the treatment of SSc-ILD.

Continuation:

- Patient received initial authorization for the requested drug; AND
- Patient will not use the requested drug in combination with nintedanib (Ofev) for the treatment of SSc-ILD; AND
- Patient is benefitting from the requested medication as supported by provider documentation
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) when any of the following criteria for their respective disease listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary:****

- For rheumatoid arthritis:
  - Patient has failed treatment with adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals], adalimumab-ryvk [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy (applicable to subcutaneous requests ONLY)
  - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths
- For systemic juvenile idiopathic arthritis:
  - Patient has inadequate clinical response to NSAIDS or corticosteroids
  - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as resolution of fever, reduction in rash or other skin manifestations, normalization of inflammatory markers (e.g., C-reactive protein or erythrocyte sedimentation rate), decreased corticosteroid requirements, reduced joint pain, stiffness, or swelling, diminished fatigue, or enhanced ability to perform daily activities

- For polyarticular juvenile idiopathic arthritis:
    - Patient has failed treatment to one or more traditional DMARDs
    - Patient has failed treatment with adalimumab (Simlandi, adalimumab-adaz, adalimumab-adbm [manufactured by Quallent Pharmaceuticals], adalimumab-ryvk [manufactured by Quallent Pharmaceuticals]) after at least TWO months of therapy (applicable to subcutaneous requests ONLY)
    - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as improved range of motion, reduced joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living, reduced corticosteroid dosage, or improvement in inflammatory serum markers
- For giant cell arteritis:
    - Patient has failed treatment with systemic corticosteroid therapy unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient
    - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with a tocilizumab product) as evidenced by improvement in clinical signs and symptoms such as decreased headache, scalp, or jaw pain, reduced fatigue, improved vision, reduced corticosteroid dosage, or improvement in inflammatory serum markers
- For systemic sclerosis associated interstitial lung disease:
    - Patient has a Forced Vital Capacity (FVC) greater than 55% of the predicted value
    - Patient has tried and failed (e.g., intolerance or inadequate response) mycophenolate mofetil after at least 6 months of therapy
    - For continuation requests: Patient is benefitting from the requested medication as supported by provider documentation

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) when patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary**).**

Based on review of available data, the Company considers the use of tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for indications other than those listed above to be **investigational.***

Based on review of available data, the Company considers the use of a dosage form of tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for indications in which it is not approved (e.g. intravenous form for systemic sclerosis associated interstitial lung disease; subcutaneous form for COVID-19) to be **investigational.***

Based on review of available data, the Company considers the use of the intravenous form of tocilizumab (Actemra), tocilizumab-bavi (Tofidence), tocilizumab-aazg (Tyenne), and tocilizumab-anoh (Avtozma) for COVID-19 in the outpatient setting to be **investigational.***

Background/Overview

Tocilizumab is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody of the immunoglobulin IgG1κ (gamma 1, kappa) subclass with a typical H2L2 polypeptide structure that is indicated for treating rheumatoid arthritis, systemic juvenile idiopathic arthritis, polyarticular juvenile idiopathic arthritis, giant cell arteritis, cytokine release syndrome, systemic sclerosis associated interstitial lung disease, and COVID-19 (in hospitalized patients). It first became available under brand name Actemra, and has since had biosimilars, Tofidence, Tyenne, and Avtozma, become available beginning in April of 2024. While Tofidence and Avtozma are currently only available in an intravenous dosage form, Tyenne is available in both SC and intravenous forms. Single-use vials containing 80 mg/4 mL, 200 mg/10 mL, or 400 mg/20 mL of tocilizumab for intravenous infusion were originally available, and in October of 2013, a subcutaneous (SC) dosage form of tocilizumab was released for the rheumatoid arthritis indication. The SC form of tocilizumab contains 162 mg of tocilizumab in 0.9 mL. This 162 mg dosage can also be used for giant cell arteritis, systemic sclerosis associated interstitial lung disease, and both systemic and juvenile idiopathic arthritis.

Dosing for tocilizumab in rheumatoid arthritis is 4 mg/kg IV every 4 weeks following by an increase to 8 mg/kg IV every 4 weeks based on clinical response. The SC dosing is weight based. In patients less than 100 kg, the dosing is 162 mg administered SC every other week, followed by an increase to every week based on clinical response. For patients at or above 100 kg, the dosing is 162 mg SC every week. Dosing for polyarticular juvenile idiopathic arthritis is weight based. If a patient is less than 30 kg, the dose is 10 mg/kg IV every 4 weeks. If the patient is at or above 30 kg, the dose is 8 mg/kg IV every 4 weeks. As of late 2018, there is a subcutaneous option for dosing for this indication. The dosing for patients less than 30 kg is 162 mg SC every three weeks. For those at or above 30 kg, the SC dose is 162 mg once every two weeks. For systemic juvenile idiopathic arthritis, the dosing is weight based as well. If the patient is less than 30 kg, the dose is 12 mg/kg IV every 2 weeks. If the patient's weight is at or above 30 kg, the dose is 8 mg/kg IV every 2 weeks. As of late 2018, there is a subcutaneous option for dosing for this indication. The dosing for patients less than 30 kg is 162 mg SC every two weeks. For those at or above 30 kg, the SC dose is 162 mg once every week. For giant cell arteritis, the dosing is 162 mg given once every week as a SC injection, in combination with a tapering course of glucocorticoids. A dose of 162 mg given once every other week can be considered. Intravenous dosing for giant cell arteritis is 6 mg/kg every 4 weeks in combination with a tapering course of glucocorticoids. Dosing for cytokine release syndrome is weight based as well. The dose for patients less than 30 kg is 12 mg/kg. For those above 30 kg of

weight is 8 mg/kg. The max dose per infusion for cytokine release syndrome is 800 mg/infusion. No more than 4 total infusions of tocilizumab should be used for cytokine release syndrome. Dosing for systemic sclerosis associated interstitial lung disease is 162 mg given once every week as a SC injection. Dosing for COVID-19 is 8 mg/kg administered by a 60 minute infusion.

Rheumatoid Arthritis
Rheumatoid Arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Polyarticular Juvenile Idiopathic Arthritis
Polyarticular juvenile idiopathic arthritis includes the inflammation of joints and presence of arthritis in children. Polyarticular juvenile idiopathic arthritis typically occurs in a symmetrical manner with knees, wrists, and ankles most frequently affected. However certain subgroups of children do have predominantly asymmetrical involvement. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Systemic Juvenile Idiopathic Arthritis
Systemic juvenile idiopathic arthritis (formerly known as Still's disease or systemic juvenile rheumatoid arthritis) is a subset of juvenile idiopathic arthritis. Patients often have intermittent fever, rash, and arthritis. The diagnosis of this condition is very difficult due to the lack of specific diagnostic tests coupled with arthritis not being present in the early form of the disease. The diagnosis is typically made clinically based upon intermittent daily, high, spiking fevers for at least two weeks and arthritis. A salmon pink rash may also be present. Typical early treatments include corticosteroids or NSAID products prior to progressing to a biologic product.

Disease-Modifying Anti-Rheumatic Drugs
Disease-modifying anti-rheumatic drugs are typically used for the treatment of rheumatoid arthritis and polyarticular juvenile idiopathic arthritis. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine
- gold compounds

Giant Cell Arteritis
Giant cell (temporal) arteritis is the most common of the systemic vasculitides and most often, occurs in those age 50 years or older. Typical presentation could include headache, abrupt visual disturbances, jaw claudication, unexplained fever or anemia, as well as elevated ESR and/or CRP. The gold standard for the diagnosis of giant cell arteritis is temporal biopsy. Typically, only a

suspicion of giant cell arteritis warrants treatment with a steroid, such as prednisone. High dose corticosteroids are recommended as the first line treatment option. The corticosteroid dose is gradually reduced to establish a maintenance dose that controls disease activity.

Cytokine Release Syndrome
T-cells can be genetically modified to target tumors through the expression of a chimeric antigen receptor. To date, the most prevalent adverse effect following infusion of CAR-T cells is the onset of immune activation, also known as cytokine release syndrome. Cytokine release syndrome has also been seen following the infusion of therapeutic monoclonal antibodies, interleukins, etc. The hallmark of cytokine release syndrome is immune activation resulting in elevated inflammatory cytokines. Clinical features include high fever, malaise, fatigue, myalgia, nausea, anorexia, tachycardia/hypotension, capillary leak, cardiac dysfunction, renal impairment, hepatic failure, and disseminated intravascular coagulation. One of the drugs that uses this technology is tisagenlecleucel (Kymriah®)‡. Kymriah's package insert defines severe or life-threatening cytokine release syndrome as having either hemodynamic instability despite intravenous fluids and vasopressor support OR worsening respiratory distress, including pulmonary infiltrates, increasing oxygen requirement including high-flow oxygen and/or need for mechanical ventilation OR rapid clinical deterioration. Lower grades of cytokine release syndrome can be treated by antibiotics, symptom support (prodromal syndrome), antipyretics, oxygen, intravenous fluids and/or low dose vasopressors (overt cytokine release syndrome). This is the definition that will be used in the medical policy. Higher degrees of cytokine release syndrome (resistant type) can be treated with additional doses of tocilizumab, multiple vasopressors, oxygen, and/or methylprednisolone. Currently, the only FDA approved product to treat CAR-T associated cytokine release syndrome is tocilizumab. No more than 4 total doses should be administered for cytokine release syndrome. The interval should be at least 8 hours between infusions and no infusion should exceed 800 mg.

Systemic Sclerosis Associated Interstitial Lung Disease (SSc-ILD)
Scleroderma is an autoimmune condition affecting the skin and other organs in the body. The main finding in scleroderma is thickening of the skin and other inflammation and scarring of many body parts. There are two major subsets of systemic sclerosis: diffuse cutaneous systemic sclerosis and limited cutaneous systemic sclerosis. As the nomenclature insinuates, the diffuse variety has extensive skin involvement. Patients with this subset are more likely to develop interstitial lung disease. Interstitial lung disease is a frequent complication of systemic sclerosis. Early interstitial lung disease is typically asymptomatic, however it is progressive and has a poor prognosis. Diagnosis involves use of HRCT without the use of contrast so as to avoid pseudo-ground-glass opacities or so-called hurricane artifacts. Treatment of this condition often includes use of an immunosuppressant, such as mycophenolate mofetil or cyclophosphamide. The Scleroderma Lung Study II compared mycophenolate mofetil with cyclophosphamide and found no difference in lung function, however there was better tolerance to mycophenolate mofetil. The only other drug approved by the FDA for this condition is Ofev.

COVID-19
Discussion of COVID-19 is beyond the scope of this medical policy as Actemra is only FDA approved for use in hospitalized patients.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Actemra was first approved in 2010 and is indicated for treating rheumatoid arthritis, systemic juvenile idiopathic arthritis, polyarticular juvenile idiopathic arthritis, giant cell arteritis, cytokine release syndrome, and systemic sclerosis associated interstitial lung disease, and COVID-19 (in hospitalized patients).

Tofidence was the first biosimilar to Actemra to be approved in September of 2023. It carries the same indications as Actemra IV, except for the cytokine release syndrome and systemic sclerosis associated interstitial lung disease indications.

Tyenne is the second biosimilar to Actemra and was approved in March of 2024. It is approved for rheumatoid arthritis, giant cell arteritis, polyarticular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, cytokine release syndrome, and COVID-19 (in hospitalized patients).

Avtozma is the third biosimilar to Actemra and was approved in July of 2025. It is approved for rheumatoid arthritis, systemic juvenile idiopathic arthritis, polyarticular juvenile idiopathic arthritis, giant cell arteritis, cytokine release syndrome, and COVID-19 (in hospitalized patients).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Rheumatoid Arthritis-Intravenous

The efficacy and safety of tocilizumab was assessed in five randomized, double-blind, multicenter studies in patients > 18 years with active rheumatoid arthritis diagnosed according to American College of Rheumatology (ACR) criteria. Patients had at least eight tender and six swollen joints at baseline. Tocilizumab was given IV every four weeks as monotherapy (Study I), in combination with methotrexate (Studies II and III) or other DMARDs (Study IV) in patients with an inadequate response to those drugs, or in combination with methotrexate in patients with an inadequate response to TNF antagonists (Study V).

Study I evaluated patients with moderate to severe active rheumatoid arthritis who had not been treated with methotrexate within six months prior to randomization, or who had not discontinued previous methotrexate treatment as a result of clinically important toxic effects or lack of response. In this study, 67% of patients were methotrexate-naïve, and over 40% of patients had rheumatoid arthritis less than two years. Patients received tocilizumab 8 mg/kg monotherapy or methotrexate alone (dose titrated over eight weeks from 7.5 mg to a maximum of 20 mg weekly). The primary endpoint was the proportion of tocilizumab patients who achieved an ACR20 response at Week 24.

Study II is an ongoing 2-year study with a planned interim analysis at week 24 that evaluated patients with moderate to severe active rheumatoid arthritis who had an inadequate clinical response to methotrexate. Patients received tocilizumab 8 mg/kg, tocilizumab 4 mg/kg, or placebo every 4 weeks, in combination with methotrexate (10 to 25 mg weekly). The primary endpoint at week 24 was the proportion of patients who achieved an ACR20 response.

Study III evaluated patients with moderate to severe active rheumatoid arthritis who had an inadequate clinical response to methotrexate. Patients received tocilizumab 8 mg/kg, tocilizumab 4 mg/kg, or placebo every 4 weeks, in combination with methotrexate (10 to 25 mg weekly). The primary endpoint was the proportion of patients who achieved an ACR20 response at week 24.

Study IV evaluated patients who had an inadequate response to their existing therapy, including one or more DMARDs. Patients received tocilizumab 8 mg/kg or placebo every 4 weeks, in combination with the stable DMARDs. The primary endpoint was the proportion of patients who achieved an ACR20 response at week 24.

Study V evaluated patients with moderate to severe active rheumatoid arthritis who had an inadequate clinical response or were intolerant to one or more TNF antagonist therapies. The TNF antagonist therapy was discontinued prior to randomization. Patients received tocilizumab 8 mg/kg, tocilizumab 4 mg/kg, or placebo every 4 weeks, in combination with methotrexate (10 to 25 mg weekly). The primary endpoint was the proportion of patients who achieved an ACR20 response at week 24.

Clinical Response
In all studies, patients treated with 8 mg/kg tocilizumab had statistically significant ACR20, ACR50, and ACR70 response rates versus methotrexate- or placebo-treated patients at week 24.

Patients treated with tocilizumab at a dose of 4 mg/kg in patients with inadequate response to DMARDs or TNF antagonist therapy had lower response rates compared to patients treated with tocilizumab 8 mg/kg.

Rheumatoid Arthritis-Subcutaneous
The efficacy and safety of SC administered tocilizumab was assessed in two double-blind, controlled, multicenter studies in patients with active rheumatoid arthritis. One study (SC-I) was a non-inferiority study that compared the efficacy and safety of tocilizumab 162 mg administered every week SC to 8 mg per kg IV every four weeks. The second study (SC-II) was a placebo-controlled superiority study that evaluated the safety and efficacy of tocilizumab 162 mg administered every other week SC to placebo. Both SC-I and SC-II required patients to be > 18 years of age with moderate to severe active rheumatoid arthritis diagnosed according to ACR criteria who had at least 4 tender and 4 swollen joints at baseline (SC-I) or at least 8 tender and 6 swollen joints at baseline (SC-II), and an inadequate response to their existing DMARD therapy, where approximately 20% also had a history of inadequate response to at least one TNF inhibitor. All patients in both SC studies received background non-biologic DMARD(s). In SC-I, 1262 patients were randomized 1:1 to receive tocilizumab SC 162 mg every week or tocilizumab IV 8 mg/kg every four weeks in combination with DMARD(s). In SC-II, 656 patients were randomized 2:1 to

tocilizumab SC 162 mg every other week or placebo, in combination with DMARD(s). The primary endpoint in both studies was the proportion of patients who achieved an ACR20 response at Week 24. In SC-I, the primary outcome measure was ACR20 at Week 24. The pre-specified non-inferiority margin was a treatment difference of 12%. The study demonstrated non-inferiority of tocilizumab with respect to ACR20 at Week 24; ACR50, ACR70, and DAS28 responses are also shown in Table 7. In SC-II, a greater portion of patients treated with tocilizumab 162 mg SC every other week achieved ACR20, ACR50, and ACR70 responses compared to placebo-treated patients. Further, a greater proportion of patients treated with tocilizumab 162 mg SC every other week achieved a low level of disease activity as measured by a DAS28-ESR less than 2.6 at Week 24 compared to those treated with placebo.

Polyarticular Juvenile Idiopathic Arthritis - Intravenous
Tocilizumab was assessed for polyarticular juvenile idiopathic arthritis in a three part study in patients who had an inadequate response to methotrexate or inability to tolerate methotrexate. The primary endpoint was the proportion of patients with a juvenile idiopathic arthritis ACR30 flare at week 40 relative to week 16. Juvenile idiopathic arthritis IA ACR 30 flare was defined as 3 or more of the 6 core outcome variables worsening by at least 30% with no more than 1 of the remaining variables improving by more than 30% relative to Week 16. Tocilizumab treated patients experienced significantly fewer disease flares compared to placebo-treated patients (26% [21/82] versus 48% [39/81]; adjusted difference in proportions -21%, 95% CI: -35%, -8%).

Polyarticular Juvenile Idiopathic Arthritis - Subcutaneous
Tocilizumab SC in polyarticular juvenile idiopathic arthritis was assessed in a 52-week, open-label, multicenter, pharmacokinetic/pharmacodynamic (PK/PD) and safety study to determine the appropriate SC dose of tocilizumab that achieved comparable PK/PD profiles to the tocilizumab IV regimen. Polyarticular juvenile idiopathic arthritis patients aged 1 to 17 years with an inadequate response or inability to tolerate methotrexate, including patients with well-controlled disease on treatment with tocilizumab IV and tocilizumab-naïve patients with active disease, were treated with tocilizumab SC based on body weight. Patients weighing at or above 30 kg (n = 25) were treated with 162 mg of tocilizumab SC every 2 weeks and patients weighing less than 30 kg (n = 27) received 162 mg of tocilizumab SC every 3 weeks for 52 weeks. The efficacy of subcutaneous tocilizumab in children 2 to 17 years of age is based on pharmacokinetic exposure and extrapolation of the established efficacy of intravenous tocilizumab in polyarticular juvenile idiopathic arthritis patients and subcutaneous tocilizumab in patients with rheumatoid arthritis.

Systemic Juvenile Idiopathic Arthritis - Intravenous
The efficacy of tocilizumab for the treatment of systemic juvenile idiopathic arthritis was assessed in a 12 week randomized, double blind, placebo controlled trial. The primary endpoint of the trial was the proportion of patients with at least 30% improvement in JIA ACR core set (JIA ACR 30 response) at Week 12 and absence of fever (no temperature at or above 37.5°C in the preceding 7 days. Eighty-five percent (85%) of patients in the tocilizumab group met the primary endpoint vs. 24% in the placebo group.

Systemic Juvenile Idiopathic Arthritis - Subcutaneous
Tocilizumab SC in pediatric patients with systemic juvenile idiopathic arthritis was assessed in a 52-week, open-label, multicenter, PK-PD and safety study to determine the appropriate subcutaneous dose of tocilizumab that achieved comparable PK/PD profiles to the tocilizumab IV regimen. Eligible patients received tocilizumab SC dosed according to body weight, with patients weighing at or above 30 kg (n = 26) dosed with 162 mg of tocilizumab every week and patients weighing below 30 kg (n = 25) dosed with 162 mg of tocilizumab every 10 days (n=8) or every 2 weeks (n=17) for 52 weeks. The efficacy of subcutaneous tocilizumab in children 2 to 17 years of age is based on pharmacokinetic exposure and extrapolation of the established efficacy of intravenous tocilizumab in systemic juvenile idiopathic arthritis patients.

Giant Cell Arteritis - Subcutaneous
The safety and efficacy of tocilizumab SC was evaluated in a single, randomized, double-blind, multicenter study in patients with active giant cell arteritis. Patients were placed in four treatment arms. Two doses of tocilizumab (162 mg once weekly and every other week) were compared to placebo (prednisone taper over 26 weeks and 52 weeks). The study consisted of a 52 week blinded period, followed by a 104 week open label extension. All patients received background prednisone therapy. The primary efficacy endpoint was the proportion of patients achieving sustained remission from week 12 thru week 52. This was defined as 1.) absence of giant cell arteritis signs and symptoms from week 12 thru week 52, 2.) normalization of erythrocyte sedimentation rate (to less than 30 mm/hr without an elevation to greater than or equal to 30 mm/hr attributable to giant cell arteritis) from week 12 to week 52, 3.) normalization of C-reactive protein to less than 1 mg/dL with an absence of successive elevations greater than or equal to 1 mg/dL from week 12 to week 52, and 4.) successful adherence to the prednisone taper defined by not more than 100 mg of excess prednisone from week 12 through week 52. Both arms of the tocilizumab treated patients showed superiority in achieving sustained remission from week 12 to week 52 compared with placebo plus 26 weeks of prednisone. Both tocilizumab arms also achieved superiority as compared to the placebo plus 52 weeks of prednisone arm. Percent responders were 14%, 17.6%, 56%, and 53.1% in the placebo plus 26 week prednisone taper, placebo plus 52 week prednisone taper, tocilizumab once weekly plus prednisone taper, and tocilizumab every other week plus prednisone taper groups.

Giant Cell Arteritis - Intravenous
Intravenously administered tocilizumab in patients with giant cell arteritis was assessed in an open-label pharmacokinetic-pharmacodynamic (PK-PD) and safety study to determine the appropriate intravenous dose of tocilizumab that achieved comparable PK-PD profiles to the tocilizumab SC regimen. At enrollment, all patients (n = 24) were in remission on intravenous tocilizumab. In Period 1, all patients received open-label intravenous tocilizumab 7 mg/kg every 4 weeks for 20 weeks. Patients who completed Period 1 and remained in remission (n = 22) were eligible to enter Period 2. They received open-label intravenous tocilizumab 6 mg/kg every 4 weeks for 20 weeks. The efficacy of intravenous tocilizumab 6 mg/kg in adult patients with giant cell arteritis is based on pharmacokinetic exposure and extrapolation to the efficacy established for subcutaneous tocilizumab in patients with giant cell arteritis.

Cytokine Release Syndrome
The efficacy or tocilizumab for the treatment of cytokine release syndrome was assessed in a retrospective analysis of pooled outcome data from clinical trials of CAR-T (chimeric antigen receptor T) cell therapies for hematological malignancies. Patients were given tocilizumab with or without additional high dose steroids. Resolution of cytokine release syndrome was defined as a lack of fever and off vasopressors for at least 24 hours. Sixty-nine percent (69%) of patients (31), achieved a response.

Systemic Sclerosis Associated Interstitial Lung Disease (SSc-ILD)
The clinical efficacy of tocilizumab was assessed in a phase 3 multicenter, randomized, double-blind, placebo controlled study in patients with systemic scleroderma (Study WA29767). A phase 2/3 multicenter, randomized, double-blind, placebo controlled study in patients with systemic scleroderma (Study WA27788) provided supportive information. Study WA29767 (NCT02453256) enrolled adult patients with systemic scleroderma defined by the 2013 American College of Rheumatology/European League Against Rheumatism classification criteria for systemic scleroderma, with onset of disease (first non-Raynaud symptom) of ≤ 5 years, modified Rodnan Skin Score (mRSS) of ≥ 10 and ≤ 35 at screening, elevated inflammatory markers (or platelets), and active disease based on at least one of the following: disease duration ≤ 18 months, increase in mRSS ≥ 3 units over 6 months, involvement of one new body area and an increase in mRSS of ≥ 2 over 6 months, or involvement of two new body areas within the previous 6 months, or presence of at least one tendon friction rub. Study WA27788 (NCT01532869) enrolled adult patients with systemic scleroderma with onset of disease ≤ 5 years, mRSS of ≥ 15 and ≤ 40 at screening, active disease, and elevated inflammatory markers or platelets. Patients in both studies were not permitted to use biologic agents (such as TNF antagonists), alkylating agents, or cyclophosphamide.

In Study WA29767, 212 patients were randomized in a 1:1 ratio to receive weekly SC injections of 162 mg of tocilizumab or placebo during the 48-week, double-blinded, placebo controlled period. Rescue treatment was allowed during the treatment period after 16 weeks for > 10% percent predicted Forced Vital Capacity (ppFVC) decline or after 24 weeks for worsening skin fibrosis. The primary efficacy endpoint was change from baseline at week 48 in mRSS. Change from baseline in FVC at week 48 was a key secondary endpoint.

In the overall population of Study WA29767, there was not a statistically significant difference in the mean change from baseline to week 48 in mRSS (primary endpoint) in patients receiving tocilizumab compared to placebo (difference: -1.73; 95% CI: -3.78, 0.32). There also was not a statistically significant effect on the primary endpoint of mRSS in Study WA27788.

In the overall population of Study WA29767, patients treated with tocilizumab, as compared to placebo treated patients, were observed to have less decline from baseline in ppFVC and observed FVC at 48 weeks. FVC results from Study WA27788 were similar.

Of the 212 patients who were randomized in Study WA29767, 68 patients (65%) in the tocilizumab arm and 68 patients (64%) in the placebo arm had SSc-ILD at baseline, as confirmed by a visual read of high resolution computed tomograph (HRCT) by blinded thoracic radiologists. The mean ppFVC at baseline for patients with SSc-ILD identified by HRCT was 79.6% (median 80.5%). Post-

hoc analyses were performed to evaluate results within the subgroups of patients with and without SSc-ILD. The ppFVC and observed FVC results in the overall population were primarily driven by results in the SSc-ILD subgroup. In the SSc-ILD subgroup, the differences in mean changes from baseline to Week 48 for tocilizumab, as compared to placebo, were 6.47% and 241 mL for ppFVC and observed FVC, respectively. The results of the key FVC secondary endpoints from Study WA29767 support a conclusion of effectiveness of tocilizumab in reducing the rate of progressive loss of lung function in the study population. However, in settings where a trial does not provide evidence of an effect on the primary endpoint, the estimated magnitude of effect on other endpoints should be interpreted with caution, and comparisons to results of other products and studies may be misleading.

COVID-19
The use of tocilizumab in patients with COVID-19 is only approved by the FDA in hospitalized patients. The clinical trials for COVID-19 are beyond the scope of this medical policy.

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Original Effective Date: 07/21/2010
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Policy History

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07/01/2010	Medical Policy Committee review
07/21/2010	Medical Policy Implementation Committee approval. New policy.
06/02/2011	Medical Policy Committee review
06/15/2011	Medical Policy Implementation Committee approval. Added new FDA indication for systemic juvenile idiopathic arthritis.
06/14/2012	Medical Policy Committee review
06/20/2012	Medical Policy Implementation Committee approval. Added a Note to the criteria for systemic juvenile idiopathic arthritis stating that patients must have had an inadequate clinical response to therapies such as nonsteroidal anti-inflammatory drugs (NSAIDS) or corticosteroids before using tocilizumab (Actemra). The reason for denial will be not medically necessary if this criterion is not met. The not medically necessary denial statement is also incorporated into the Investigational and Not Medically Necessary coverage sections. Deleted the investigational statement regarding non-FDA approved indications, since it is duplicative given the additions to the coverage section.
11/01/2012	Medical Policy Committee review
11/28/2012	Medical Policy Implementation Committee approval. Added new FDA approved indication.
06/06/2013	Medical Policy Committee review
06/25/2013	Medical Policy Implementation Committee approval. Changed some wording to match other similar policies. Added a new indication of polyarticular juvenile idiopathic arthritis with similar criteria as other drugs. Relocated PPD to each indication instead of a note. Reworded the Investigational and Not Medically Necessary sections. Updated some background info.
12/12/2013	Medical Policy Committee review
12/18/2013	Medical Policy Implementation Committee approval. Added requirements for Actemra SubQ requests to have tried both Humira and Enbrel. Updated Investigational and Not Medically Necessary sections to reflect change. Updated Background/Overview info and Rationale/Source sections to reflect new subQ dosage form of Actemra.
12/04/2014	Medical Policy Committee review
12/17/2014	Medical Policy Implementation Committee approval. No change to coverage.
12/03/2015	Medical Policy Committee review
12/16/2015	Medical Policy Implementation Committee approval. No change to coverage.
12/01/2016	Medical Policy Committee review
12/21/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
08/03/2017	Medical Policy Committee review
08/23/2017	Medical Policy Implementation Committee approval. Added indication and information for Giant Cell Arteritis. Clarified TB test. Updated language for combo use of biologics.

11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. Removed requirement for Humira and Enbrel prior to Actemra for RA. Added the new FDA approved indication for cytokine release syndrome and subsequent background info and updates.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Updated to reflect the new availability of subcutaneous dosing for both systemic and polyarticular juvenile idiopathic arthritis. For the polyarticular variety, the use of Humira will be required first. Updated background information and rationale/source to reflect the new dosage.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. For rheumatoid arthritis subcutaneous Actemra requests, added a requirement for Humira failure first.
10/01/2021	Coding update
12/02/2021	Medical Policy Committee review
12/08/2021	Medical Policy Implementation Committee approval. Updated the policy with a new FDA approved indication, systemic sclerosis associated interstitial lung disease (SSc-ILD), along with coverage criteria and background information.
12/01/2022	Medical Policy Committee review
12/14/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Updated the giant cell arteritis criteria to include use of the IV version, which was recently an FDA approved route of administration. Added the dosage limit for the IV version for giant cell arteritis. Added an investigational statement for use in COVID-19 outside of hospitalized patients.
09/05/2024	Medical Policy Committee review
09/11/2024	Medical Policy Implementation Committee approval. Changed title of policy from “tocilizumab (Actemra)” to “tocilizumab Products” to reflect availability of biosimilar products. Added biosimilars, Tyenne and Tofidence, to policy with criteria. Updated relevant sections.
09/16/2024	Coding update.
09/04/2025	Medical Policy Committee review
09/10/2025	Medical Policy Implementation Committee approval. Added continuation criteria to the RA, PJIA, and SJIA indications. Updated age requirement for GCA from 50 to 18 years of age. Updated criteria to clarify that doses above the labeled maximum dose are considered investigational.
10/01/2025	Coding update.
11/01/2025	Coding update.

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12/04/2025 Medical Policy Committee review
12/10/2025 Medical Policy Implementation Committee approval. Added new product, Avtozma, to the policy with criteria and updated relevant sections where needed. Updated preferred alternatives by removing brand Humira from the list of options and adding in the Quallent Pharmaceuticals products. Updated continuation criteria to clarify that doses above the labeled maximum dose are considered investigational.
Next Scheduled Review Date: 12/2026

Coding

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3262, Q5133, Q5135, Q5156
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.