Washington State Health Care Authority

Cytokine and CAM Antagonists: IL-6 Inhibitors

Medical policy no. 66.27.00.AC-4 Effective Date: Month, 1, Year

Related medical policies:

Policy Number	Policy Name
66.27.00.AA	Cytokine and CAM Antagonists: Tumor Necrosis Factor (TNF) Inhibitors
66.27.00.AB	Cytokine and CAM Antagonists: IL-4/IL-13 Inhibitors
66.27.00.AD	Cytokine and CAM Antagonists: IL-12/IL-23 Inhibitors
66.27.00.AE	Cytokine and CAM Antagonists: IL-17 Inhibitors
66.27.00.AF	Cytokine and CAM Antagonists: Oral PDE-4 Inhibitors
66.27.00.AG	Cytokine and CAM Antagonists: T-Lymphocyte Inhibitors
66.27.00.AH	Cytokine and CAM Antagonists: Janus Associated Kinase (JAK) Inhibitors
66.27.00.AI	Cytokine and CAM Antagonists: IL-1 Inhibitors
66.27.00.AJ	Cytokine and CAM Antagonists: Integrin Receptor Antagonists
66.27.00.AK	Cytokine and CAM Antagonists: S1-P Receptor Modulator

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
Sarilumab (Kevzara) Tocilizumab (Actemra) <u>Tocilizumab biosimilars:</u> Tocilizumab-aazg (Tyenne) Tocilizumab-bavi (Tofidence)	**IL-6 Inhibitors – sarilumab, tocilizumab** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health. Patients new to Apple Health or new to an MCO who are requesting regimens for continuation of therapy are reviewed following the reauthorization criteria listed below.

Clinical policy:

Clinical Criteria	
Polymyalgia Rheumatica (PMR) Sarilumab (Kevzara)	Sarilumab (Kevzara) may be approved when all the following documented criteria are met: 1. Patient is 50 years of age or older; **AND** 2. Prescribed by, or in consultation with a rheumatologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Diagnosis of Polymyalgia Rheumatica; **AND** 5. Presence of ALL the following: a. Bilateral shoulder or pelvic girdle pain lasting at least 2 weeks; **AND** b. Morning stiffness for greater than 45 minutes; **AND** c. Elevated C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR); **AND** 6. History of failure, contraindication, or intolerance to at least one glucocorticoid (i.e., prednisone, hydrocortisone, methylprednisolone, etc.) and attempted dose reduction/taper has been ineffective, contraindicated, or not tolerated [minimum trial of 2 months] If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Sarilumab (Kevzara) may be approved when all the following documented criteria are met: **1.** Not used in combination with another Cytokine and CAM medication; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., reduction of elevated inflammatory markers the CRP and ESR, improvement of bilateral shoulder and/or pelvic girdle pain, reduction of duration of daily morning stiffness). If ALL criteria are met, the request will be authorized for **12 months.**
Giant Cell Arteritis (GCA) Tocilizumab (Actemra) Tocilizumab biosimilars	Tocilizumab (Actemra) and tocilizumab biosimilars may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Prescribed by, or in consultation with a rheumatologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Documentation of current weight is provided; **AND** 5. Diagnosis of Giant Cell Arteritis (GCA); **AND**

	6. Presence of at least <u>three</u> of the following: a. Age at disease onset of at least 50 years; **OR** b. New onset headache at time of diagnosis; **OR** c. Temporary artery abnormality (tenderness to palpation or decreased pulsation); **OR** d. Elevated ESR; **OR** e. Abnormal artery biopsy; **AND** 7. History of failure, contraindication, or intolerance to at least one glucocorticoid (i.e., prednisone, hydrocortisone, methylprednisolone, etc.) If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Not used in combination with another Cytokine and CAM medication; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g. improve in headache, temporal artery tenderness, visual symptoms, steroid free clinical remission, CRP, ESR). If ALL criteria are met, the request will be authorized for **12 months.**
Rheumatoid Arthritis Sarilumab (Kevzara) Tocilizumab (Actemra) Tocilizumab biosimilars	Sarilumab (Kevzara), tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Prescribed by, or in consultation with a rheumatologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. For tocilizumab, documentation of current weight is provided; **AND** 5. Diagnosis of Rheumatoid Arthritis (RA); **AND** 6. Baseline assessments are included (e.g., Disease Activity Score for 28 joints (DAS28) with the CRP, DAS28 with ESR, Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Routine Assessment of Patient Index Data 3 (RAPID3), Patient Activity Scale (PAS) II; **AND** 7. Treatment with at least one non-Cytokine and CAM DMARD (e.g., methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, cyclosporine, azathioprine) have been ineffective, contraindicated, or not tolerated [minimum trial of 3 months] 8. Treatment with two preferred Cytokine & CAM Apple Health Preferred Drug List (AHPDL) medications has each been ineffective, contraindicated, or not tolerated [minimum trial of 12 weeks]. If ALL criteria are met, the request will be authorized for **6 months.**

	Criteria (Reauthorization) Sarilumab (Kevzara), tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Not used in combination with another Cytokine and CAM medication; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g. improvement in DAS28 with CRP/ESR, SDAI, CDAI, RAPID3, PAS II scores). If ALL criteria are met, the request will be authorized for **12 months.**
Polyarticular Juvenile Idiopathic Arthritis (PJIA) Tocilizumab (Actemra) Tocilizumab biosimilars	Tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Patient is 2 to 17 years of age; **AND** 2. Prescribed by, or in consultation with a rheumatologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Diagnosis of Polyarticular Juvenile Idiopathic Arthritis (PJIA); **AND** 5. Documentation of current weight is provided; **AND** 6. Treatment with at least one non-Cytokine and CAM DMARD (e.g., methotrexate, sulfasalazine, leflunomide, hydroxychloroquine, azathioprine, cyclosporine) have been ineffective, contraindicated, or not tolerated [minimum trial of 3 months] 7. Treatment with two preferred Cytokine & CAM Apple Health Preferred Drug List (AHPDL) medications has each been ineffective, contraindicated, or not tolerated [minimum trial of 12 weeks]. If ALL criteria are met, the request will be authorized for **6 months.** **Criteria (Reauthorization)** Tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Not used in combination with another Cytokine and CAM medication; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., improvement in joint pain, swelling, activities of daily living, reduction in diseases flares, etc.). If ALL criteria are met, the request will be authorized for **12 months.**

Systemic Juvenile Idiopathic Arthritis Tocilizumab (Actemra) Tocilizumab biosimilars	Tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Patient is 2 to 17 years of age; **AND** 2. Documentation of current weight is provided; **AND** 3. Prescribed by, or in consultation with a rheumatologist; **AND** 4. Not used in combination with another Cytokine and CAM medication; **AND** 5. Diagnosis of active systemic juvenile idiopathic arthritis (SJIA); **AND** 6. Patient has severe active disease as indicated by one of the following: a. Suspected early macrophage activating syndrome (MAS); **OR** b. Disabling polyarthritis; **OR** c. Serositis; **AND** 7. History of failure, contraindication, or intolerance to one of the following: a. NSAID (e.g., ibuprofen, naproxen, indomethacin, meloxicam, celecoxib, etc.) [minimum trial of 1 week]; **OR** b. Glucocorticoid (i.e., prednisone, hydrocortisone, methylprednisolone, etc.) [minimum trial of 2 weeks]; **AND** 8. Treatment with at least one non-Cytokine and CAM disease-modifying antirheumatic drug (DMARD) (e.g., methotrexate, leflunomide, cyclosporine, thalidomide) has been ineffective, contraindicated, or not tolerated [minimum trial of 3 months]. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Not used in combination with another Cytokine and CAM medication; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g. improvement in joint pain or stiffness) If ALL criteria are met, the request will be authorized for **12 months.**
Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) Tocilizumab (Actemra)	Tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older; **AND** 2. Prescribed by, or in consultation with a pulmonologist; **AND**

	3. Not used in combination with nintedanib (Ofev) or pirfenidone (Esbriet); **AND** 4. Diagnosis of Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD); **AND** 5. Diagnosis is confirmed by a high resolution computed tomographic (HRCT) scan; **AND** 6. Treatment with at least one immunomodulator (e.g., mycophenolate or cyclophosphamide) have been ineffective, contraindicated, or not tolerated [minimum trial of 3 months] If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Tocilizumab (Actemra) may be approved when all the following documented criteria are met: 1. Not used in combination with nintedanib (Ofev) or pirfenidone (Esbriet); **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g., sustained forced vital capacity (%FVC) decline or minimal decline in diffusing capacity of the lung for carbon monoxide (DLCO)) If ALL criteria are met, the request will be authorized for **12 months.**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
Tocilizumab (Actemra) Tocilizumab biosimilars (Tofidence, Tyenne)	Giant cell arteritis	6 mg/kg IV every 4 weeks; max 600 mg IV per infusion 162 mg subQ once weekly	• 162mg/0.9ml autoinjector pens or PFS; 4 per 28 day supply • 80mg/4ml SDV (#1 per box); 1 per 14 days • 200 mg/10ml SDV (#1 per box); 3 per 28 days • 400 mg/20ml SDV (#1 per box); 2 per 14 days
	Rheumatoid arthritis	4-8 mg/kg IV infusion every 4 weeks; doses > 800 mg are not recommended Weight < 100 kg: 162 mg subQ every other week	• Weight < 100 kg: 162mg/0.9ml autoinjector pens or PFS; 2 per 28 day supply • Weight ≥ 100 kg: 162mg/0.9ml autoinjector pens or PFS; 4 per 28 day supply • 80mg/4ml SDV (#1 per box); 1 per 14 days

		Weight ≥ 100 kg: 162 mg subQ every week	• 200 mg/10ml SDV (#1 per box); 3 per 28 days • 400 mg/20ml SDV (#1 per box); 2 per 14 days
	Polyarticular juvenile idiopathic arthritis	2 years or older, < 30 kg: • IV: 10 mg/kg every 4 weeks • subQ: 162 mg once every 3 weeks 2 years or older, ≥ 30 kg: • IV: 8 mg/kg every 4 weeks • subQ: 162 mg once every 2 weeks	• Weight < 30 kg: 162mg/0.9ml autoinjector pen or PFS; 1 per 21 day supply • Weight ≥ 30 kg: 162mg/0.9ml autoinjector pens or PFS; 2 per 28 day supply • 80mg/4ml SDV (#1 per box); 1 per 14 days • 200 mg/10ml SDV (#1 per box); 3 per 28 days • 400 mg/20ml SDV (#1 per box); 2 per 14 days
	Systemic juvenile idiopathic arthritis	2 years or older, < 30 kg: • IV: 12 mg/kg every 2 weeks • subQ: 162 mg once every 2 weeks 2 years or older, ≥ 30 kg: • IV: 8 mg/kg every 2 weeks • subQ: 162 mg once every week	• Weight < 30 kg: 162mg/0.9ml autoinjector pens or PFS; 2 per 28 day supply • Weight ≥ 30 kg: 162mg/0.9ml autoinjector pens or PFS; 4 per 28 day supply • 80mg/4ml SDV (#1 per box); 1 per 14 days • 200 mg/10ml SDV (#1 per box); 3 per 28 days • 400 mg/20ml SDV (#1 per box); 2 per 14 days
	Systemic sclerosis-associated interstitial lung disease	162 mg subQ once weekly	• 162mg/0.9ml autoinjector pens or PFS; 4 per 28 day supply
Kevzara	Polymyalgia rheumatica	200 mg subQ once every 2 weeks	• 150mg/1.14mL 2 pens or PFS per 28 day supply • 200mg/1.14mL 2 pens or PFS per 28 day supply
	Rheumatoid arthritis	200 mg subQ once every 2 weeks	• 150mg/1.14mL 2 pens or PFS per 28 day supply 200mg/1.14mL 2 pens or PFS per 28 day supply

Coding:

HCPCS Code	Description
J3262	Injection, tocilizumab, 1 billable unit = 1 mg
Q5133	Injection, tocilizumab-bavi (tofidence), biosimilar, 1 mg

Background:

Polymyalgia Rheumatica (PMR)

Polymyalgia rheumatica (PMR) is an inflammatory condition. According to the European League Against Rheumatism/American College of Rheumatology Collaborative Initiative (EULAR/ACR) classification criteria, patients are required to be age 50 years or older to be considered for a diagnosis of PMR. Other hallmark characteristics or predictors of this disease include bilateral shoulder and/or hip pain, presence of morning stiffness for greater than 45 minutes and elevation of acute phase reactants, CRP and/or ESR. Sarilumab is FDA-approved for adult patients with PMR based on results of the SAPHYR study. Sustained remission rate was significantly higher in the sarilumab arm vs the placebo arm (28.3% vs 10.3%; P = 0.0193). Trial of a corticosteroid (e.g. prednisone) is considered first-line therapy and the standard of care for patients diagnosed with PMR.

Giant Cell Arteritis

Giant Cell Arteritis (GCA, also known as Horton disease, cranial arteritis, and temporal arteritis) is the most common systemic vasculitis in North America and Europe. GCA only affects older adults with a peak incidence between age 70-79. Patients diagnosed with GCA may be at great risk of sudden vision loss. The 2021 American College of Rheumatology guidelines for GCA recommends starting high dose daily glucocorticoids, or tocilizumab with glucocorticoids, or tocilizumab alone in newly diagnosed patients. Tocilizumab is FDA approved for adult patients with giant cell arteritis based on the results of phase 3 RCT. The primary outcome in this study was the rate of sustained remission of disease comparing tocilizumab weekly and every other week combined with a 26-week corticosteroid taper compared with placebo and a 26-week or 52-week corticosteroid taper. The sustained remission response was higher in the treatment arms (56% in weekly dosing and 53% in bi-weekly dosing) compared to 14% and 18% in placebo arms, respectively.

Rheumatoid Arthritis

The 2021 American College of Rheumatology (ACR) guidelines for rheumatoid arthritis strongly recommend the use of conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapy (methotrexate preferred) in patients who are DMARD-naïve with moderate-to-severe RA. Recommended csDMARDs include methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide. In DMARD-naïve patients with moderate-to-severe disease activity, methotrexate monotherapy is strongly recommended over the addition of non-TNF inhibitor or tsDMARD based on additional risks of adding a biologic or tsDMARD and low quality data evaluating superiority over methotrexate monotherapy. The 2019 European League Against Rheumatism (EULAR) guidelines follow similar recommendations to the 2021 ACR guidelines, and state that patients with highly active RA despite treatment with csDMARDs may receive a biologic DMARD or JAK inhibitor based on high level of evidence.

Juvenile Idiopathic Arthritis

Juvenile idiopathic arthritis (JIA) is a grouping of inflammatory disorders that affect children. Polyarticular juvenile idiopathic arthritis (PJIA) is a subset of JIA, which is defined by the presence of arthritis in five or more joints during the first six months of illness. Other subsets of JIA include ERA, oligoarthritis (less than five joints affected), systemic juvenile idiopathic arthritis (SJIA; fever, rash, hepatic/splenic/lymphatic involvement) and psoriatic arthritis (psoriasis and dactylitis). While these are distinct disease states, their pathogenesis and presentation are similar so there is significant overlap in effective treatments. The 2019 American College of Rheumatology/Arthritis Foundation (ACR) guidelines for non-systemic polyarthritis (PJIA) strongly recommend initial therapy with a DMARD for all patients with JIA and active polyarthritis; methotrexate has the strongest evidence, but sulfasalazine and leflunomide can also be used. Regardless of disease activity, initial therapy with a DMARD is recommended over a biologic, though there may be certain situations where a biologic as initial therapy is preferred (i.e., high risk joints such as cervical spine, wrist, or hip involved). For patients with continued moderate to high disease activity, the guidelines recommend adding a TNF inhibitor, abatacept, or tocilizumab as second-line.

Systemic Sclerosis-Associated Interstitial Lung Disease

Scleroderma-associated interstitial lung disease (SSc-ILD) is a chronic lung disease in which fibrosis builds up in the lungs in a person diagnosed with systemic sclerosis (SSc). Direct pulmonary involvement in SSc is the main cause of death in patients with SSc. The presence of SSc-ILD is defined by the identification of fibrotic features on high-resolution CT scan. The European expert consensus published in 2020 recommends immunosuppressive therapies in severe or progressive ILD, including mycophenolate mofetil, cyclophosphamide, or nintedanib (Ofev) in patients requiring pharmacotherapy. The FDA has approved tocilizumab (Actemra) for slowing rate of decline in pulmonary function in adult patients with SSc-ILD. There is no evidence to suggest that combination therapy of tocilizumab and nintedanib or pirfenidone will be safe or effective when used to treat-SSc-ILD.

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History

Approved Date	Effective Date	Version	Action and Summary of Changes
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	Pending Approval (draft/unpublished version) -Updated clinical criteria for indication A to require Lab A. -Added indication for X. -Added new products in class which include Drug A and Drug B. -Updating dosing for Drug A. -Updating language at header note to include "If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling."
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	Approved by HCA. Updated dosing limits for expanded indication for drug X.
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	Approved by DUR Board.