Cytokine and CAM Antagonists: IL-1 Inhibitors

WA.PHAR.49.AI Effective Date: 3/1/2025

Related medical policies:

Policy Number	Policy Name
WA.PHAR.49.AA	Cytokine and CAM Antagonists: Tumor Necrosis Factor (TNF) Inhibitors
WA.PHAR.49.AB	Cytokine and CAM Antagonists: IL-4/IL-13 Inhibitors
WA.PHAR.49.AC	Cytokine and CAM Antagonists: IL-6 Inhibitors
WA.PHAR.49.AD	Cytokine and CAM Antagonists: IL-12/IL-23 Inhibitors
WA.PHAR.49.AE	Cytokine and CAM Antagonists: IL-17 Inhibitors
WA.PHAR.49.AF	Cytokine and CAM Antagonists: Oral PDE-4 Inhibitors
WA.PHAR.49.AG	Cytokine and CAM Antagonists: T-Lymphocyte Inhibitors
WA.PHAR.49.AH	Cytokine and CAM Antagonists: Janus Associated Kinase (JAK) Inhibitors
WA.PHAR.49.AJ	Cytokine and CAM Antagonists: Integrin Receptor Antagonists
WA.PHAR.49.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 publication of the Coordinated Care of Washington, Inc. Preferred Drug List (PDL), please visit: *https://www.coordinatedcarehealth.com/content/dam/centene/centene-pharmacy/pdl/FORMULARY-CoordinatedCare_Washington.pdf*

Medical necessity

Drug	Medical Necessity
Anakinra (Kineret) Canakinumab (Ilaris) Rilonacept (Arcalyst)	**Anakinra (Kineret), canakinumab (Ilaris), rilonacept (Arcalyst)** 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.

Clinical policy:

Policy: IL 1 Inhibitors (anakinra, canakinumab, rilonacept)

Clinical Criteria	
Cryopyrin-Associated Periodic Syndromes (CAPS) Anakinra (Kineret) Canakinumab (Ilaris) Rilonacept (Arcalyst)	Anakinra (Kineret), canakinumab (Illaris), and rilonacept (Arcalyst) may be approved when all the following documented criteria are met: 1. The patient meets the appropriate age limit for the requested product: a. For canakinumab: 4 years of age or older; **OR** b. For rilanocept: 12 years of age or older; **OR** c. For anakinra: no age minimum; **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 cryopyrin-associated periodic syndrome (CAPS) including the following: a. Neonatal-onset multisystem inflammatory disease (NOMID); **OR** b. Familial cold autoinflammatory syndrome (FCAS); **OR** c. Muckle-Wells Syndrome (MWS); **AND** 5. Laboratory testing showing a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1), also known as NLRP; **AND** 6. Baseline assessments are included (e.g., C-reactive protein (CRP), serum amyloid A, rash frequency). If ALL criteria are met, the request will be authorized for **6 months.** **Criteria (Reauthorization)** Anakinra (Kineret), canakinumab (Ilaris), and rilonacept (Arcalyst) 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 CRP, serum amyloid A, rash frequency). If ALL criteria are met, the request will be authorized for **12 months.**
Rheumatoid Arthritis Anakinra (Kineret)	Anakinra (Kineret) 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. Diagnosis of rheumatoid arthritis; **AND** 5. 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

	6. Treatment with at least one non-Cytokine and CAM DMARD (e.g., methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, cyclosporine, azathioprine) has been ineffective, unless all are contraindicated, or not tolerated [minimum trial of 3 months] 7. Treatment with one preferred adalimumab biosimilar and etanercept has each been ineffective, unless all are contraindicated, or not tolerated [minimum trial of 12 weeks]. If ALL criteria are met, the request will be authorized for **6 months.** **Criteria (Reauthorization)** Anakinra (Kineret) 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.**
Systemic Juvenile Idiopathic Arthritis (SJIA) Canakinumab (Ilaris) **Adult Onset Still's Disease (AOSD)** Canakinumab (Ilaris)	Canakinumab (Ilaris) may be approved when all the following documented criteria are met: 1. The patient meets the appropriate age limit and indication for the requested product: a. For active systemic juvenile idiopathic arthritis (SJIA): 2 years of age or older; **OR** b. For adult onset Still's Disease (AOSD): 18 years or age of older; **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 either of the following: a. Active systemic juvenile idiopathic arthritis (SJIA); **OR** b. Adult onset Still's Disease (AOSD); **AND** 6. Patient has severe active disease as indicated by one of the following: a. Suspected early macrophage activating syndrome (MAS) b. Disabling polyarthritis c. Serositis; **AND** 7. History of failure to ONE of the following unless all are contraindicated or not tolerated: a. NSAID (e.g., ibuprofen, naproxen, indomethacin, meloxicam, celecoxib, etc.) [minimum trial of 1 week]; **OR** b. Glucocorticoid (e.g., 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, unless all are contraindicated, or not tolerated [minimum trial of 3 months]. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Canakinumab (Ilaris) 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.**
Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) Canakinumab (Ilaris)	Canakinumab (Ilaris) may be approved when all the following documented criteria are met: 1. Patient is 2 years of age or older, **AND** 2. Prescribed by, or in consultation with an immunologist or rheumatologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Diagnosis of Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS); **AND** 5. Documentation of TNFRSF1A gene mutation; **AND** 6. Patient has chronic or recurrent fever flares, defined by three or more flares a year; **AND** a. Documentation of fever flares that last FIVE days or more; **AND** b. Fever flares are accompanied by at least ONE of the following symptoms: i. Myalgia; **OR** ii. Rash; **OR** iii. Eye symptoms (e.g., conjunctivitis, periorbital edema); **OR** iv. Limb pain; **OR** v. Abdominal symptoms (e.g., pain, vomiting); **OR** vi. Lymphadenopathy; **OR** vii. Chest pain; **AND** 7. Causes of recurrent fever have been ruled out (e.g., recurrent bacterial/viral infection, cyclic neutropenia, interferonopathies, etc). If ALL criteria are met, the request will be authorized for **6 months.**

	Criteria (Reauthorization) Canakinumab (Ilaris) 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 in fever flares) If ALL criteria are met, the request will be authorized for **12 months.**
Familial Mediterranean Fever Canakinumab (Ilaris)	Canakinumab (Ilaris) may be approved when all the following documented criteria are met: 1. Patient is 2 years of age or older, **AND** 2. Prescribed by, or in consultation with a rheumatologist or immunologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Diagnosis of familial mediterranean fever; **AND** 5. Patient has recurrent febrile episodes accompanied by at least ONE of the following: a. Peritonitis; **OR** b. Synovitis or pleuritis; **OR** c. Erysipelas-like erythema; **OR** d. First degree relative with Familial Mediterranean Fever; **AND** 6. Causes of recurrent fever have been ruled out (e.g., recurrent bacterial/viral infection, cyclic neutropenia, interferonopathies, etc.); **AND** 7. History of failure, contraindication, or intolerance to colchicine [minimum trial of 3 months]. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Anakinra (Kineret), canakinumab (Ilaris) 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 in febrile episodes) If ALL criteria are met, the request will be authorized for **12 months.**
	Canakinumab (Ilaris) may be approved when all the following documented criteria are met:

Hyperimmunoglobulin D Syndrome/Mevalonate Kinase Deficiency (HIDS/MKD) Canakinumab (Ilaris)	1. Patient is 2 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 Hyperimmunoglobulin D Syndrome/Mevalonate Kinase Deficiency (HIDS/MKD); **AND** 5. Documentation of either of the following: a. Elevated immunoglobulin D (IgD) levels; **OR** b. Documentation of V3771 mutation in the mevalonate kinase gene; **AND** 6. Documentation of fever flares that last four days or more; **AND** 7. Fever flares are accompanied by at least ONE of the following symptoms: a. Chills b. Cervical lymphadenopathy c. Abdominal symptoms (e.g., pain, vomiting, diarrhea) d. Lymphadenopathy; **AND** 8. Causes of recurrent fever have been ruled out (e.g., recurrent bacterial/viral infection, cyclic neutropenia, interferonopathies, etc.) If ALL criteria are met, the request will be authorized for **6 months.** **Criteria (Reauthorization)** Canakinumab (Ilaris) 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 in fever flares) If ALL criteria are met, the request will be authorized for **12 months.**
Recurrent Pericarditis Rilonacept (Arcalyst)	Rilonacept (Arcalyst) may be approved when all the following documented criteria are met: 1. Patient is 12 years of age or older, **AND** 2. Prescribed by, or in consultation with a cardiologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Patient has a history of three or more episodes of pericarditis; **AND** 5. Baseline assessments are included (e.g. white blood cell count (WBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) ECG); **AND** 6. History of failure to ALL of the following unless all are contraindicated, or not tolerated:

	a. NSAID or aspirin (e.g., ibuprofen, indomethacin) [minimum trial of 2 weeks] b. Colchicine [minimum trial of 12 weeks] c. Corticosteroids (e.g., prednisone) [minimum trial of 2 weeks]. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Rilonacept (Arcalyst) 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 pleuritic chest pain and ECG changes). If ALL criteria are met, the request will be authorized for **12 months.**
Gout Flare Canakinumab (Ilaris)	Canakinumab (Ilaris) 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. Patient has experienced ≥ 2 gout flares within the previous 12 months; **AND** 5. History of failure to ALL of the following unless all are contraindicated, or not tolerated: a. Non-steroidal anti-inflammatory drugs (NSAIDs) (e.g., naproxen, indomethacin, diclofenac, meloxicam, celecoxib) [minimum trial of 2 weeks] b. Colchicine [minimum trial of 12 weeks] c. Intraarticular or oral glucocorticoids (e.g. methylprednisolone acetate, triamcinolone acetonide, prednisone, prednisolone) [minimum trial of 1 week]. If ALL criteria are met, the request will be authorized for **3 months.**
	Criteria (Reauthorization) Canakinumab (Ilaris) may be approved when all the following documented criteria are met: 1. Not used in combination with other another Cytokine and CAM medication; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response (e.g. reduction in gout flares); **AND**

	3. Patient has not received treatment with canakinumab in the previous 12 weeks. If ALL criteria are met, the request will be authorized for **3 months.**
Deficiency of IL-1 Receptor Antagonist (DIRA) Anakinra (Kineret) Rilonacept (Arcalyst)	Anakinra (Kineret) and rilonacept (Arcalyst) may be approved when all the following documented criteria are met: 1. The patient meets the appropriate age limit for the requested product: a. For rilanocept: 12 years of age or older; **OR** b. For anakinra: no age minimum; **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 deficiency of IL-1 receptor antagonist; **AND** 5. Documentation of mutation in the *IL1RN* gene; **AND** 6. Baseline assessments are included (e.g. erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) ECG, skin biopsy, MRI, X-rays); AND 7. Patient experiences at least one of the following symptoms: a. Pustular psoriasis-like rash; **OR** b. Sterile osteomyelitis (i.e., rib flaring and cloaking of the femoral head, odontoid lesions); **OR** c. Nail changes (i.e., onychomadesis); **AND** If ALL criteria are met, the request will be authorized for **6 months.** **Criteria (Reauthorization)** Anakinra (Kineret), rilonacept (Arcalyst) 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 rash and x-rays) If ALL criteria are met, the request will be authorized for **12 months.**
Schnitzler Syndrome Anakinra (Kineret)	Anakinra (Kineret) 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 dermatologist, immunologist or rheumatologist; **AND** 3. Not used in combination with another Cytokine and CAM medication; **AND** 4. Diagnosis of Schnitzler Syndrome; **AND** 5. Documentation of monoclonal immunoglobulin (IgM) gammopathy; **AND** 6. Presence of a chronic urticaria-like rash

	If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization)
	Anakinra (Kineret) 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 rash) 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
Arcalyst	Cryopyrin associated periodic syndrome	**Adult dosing** Loading dose: 320 mg subQ ; then 160 mg subQ once weekly **Pediatric dosing** (12-17 years of age) Loading dose: 4.4 mg/kg subQ (MAX 320 mg); then 2.2 mg/kg (MAX 160 mg) subQ once weekly	Loading dose • 220mg/20mL vial: 2 vials Maintenance dose • 220mg/20mL vial: 4 vials per 28 days
	Deficiency of interleukin-1 receptor antagonist, Maintenance of remission	**Adult dosing** 320 mg subQ once weekly **Pediatric dosing** (10 kg or more) 4.4 mg/kg subQ once weekly (MAX 320 mg)	• 220mg/20mL vial: 8 vials per 28 days
	Recurrent pericarditis	**Adult dosing** Loading dose: 320 mg subQ ; then 160 mg subQ once weekly **Pediatric dosing** (12-17 years of age) Loading dose: 4.4 mg/kg subQ (MAX 320 mg); then 2.2 mg/kg (MAX 160 mg) subQ once weekly	Loading dose • 220mg/20mL vial: 2 vials Maintenance dose • 220mg/20mL vial: 4 vials per 28 days
Ilaris	Adult onset Still's disease	4 mg/kg subQ every 4 weeks (MAX 300 mg/dose)	• 150 mg single-dose vial: 300 billable units per 28 days

	Systemic onset juvenile chronic arthritis	2 years or older; 7.5 kg or greater: 4 mg/kg subQ every 4 weeks (MAX 300 mg/dose)	• 150 mg single-dose vial: 300 billable units per 28 days
	Cryopyrin associated periodic syndrome	Adult and pediatric dosing (4 years or older) 15 to 40 kg: 2mg/kg subQ every 8 weeks Greater than 40 kg: 150 subQ every 8 weeks	• 150 mg single-dose vial: 150 billable units per 56 days
	Deficiency of mevalonate kinase	Less than 40 kg: 2 mg/kg subQ every 4 weeks; may increase to 4 mg/kg every 4 weeks Greater than 40 kg: 150 mg subQ every 4 weeks; may increase to 300 mg subQ every 4 weeks	• 150 mg single-dose vial: 300 billable units per 28 days
	Familial cold urticaria	Adult dosing 15 to 40 kg: 2 mg/kg subQ every 8 weeks Greater than 40 kg: 150 mg subQ every 8 weeks	• 150 mg single-dose vial: 150 billable units per 56 days
	Familial Mediterranean fever	Adult dosing Less than 40 kg: 2 mg/kg subQ every 4 weeks; may increase to 4 mg/kg every 4 weeks Greater than 40 kg: 150 mg subQ every 4 weeks; may increase to 300 mg every 4 weeks	• 150 mg single-dose vial: 300 billable units per 28 days
	Hyperimmunoglobulinemia D with periodic fever	Adult dosing Less than 40 kg: 2 mg/kg subQ every 4 weeks; may increase to 4 mg/kg every 4 weeks Greater than 40 kg: 150 mg subQ every 4 weeks; may increase to 300 mg every 4 weeks	• 150 mg single-dose vial: 300 billable units per 28 days
	Muckle-Wells syndrome	Adult dosing 15 to 40 kg: 2 mg/kg subQ every 8 weeks Greater than 40 kg: 150 mg subQ every 8 weeks	• 150 mg single-dose vial: 150 billable units per 56 days

	TNF receptor-associated periodic fever syndrome	Adult dosing Less than 40 kg: 2 mg/kg subQ every 4 weeks; may increase to 4 mg/kg every 4 weeks Greater than 40 kg: 150 mg subQ every 4 weeks; may increase to 300 mg subQ every 4 weeks	• 150 mg single-dose vial: 300 billable units per 28 days
	Gout, acute	150 mg subQ once; may be repeated after an interval of at least 12 weeks for patients requiring re-treatment	• 150 mg single-dose vial: 150 billable units per 84 days
Kineret	Chronic infantile neurological, cutaneous, and articular syndrome	Initial, 1-2 mg/kg subQ once daily, may increase in 0.5 to 1 mg/kg increments to MAX 8 mg/kg/day	• 100mg/0.67mL PFS: weight-based dosing
	Deficiency of interleukin-1 receptor antagonist		
	Rheumatoid arthritis	100 mg/day subQ	• 100mg/0.67mL PFS: 28 PFS per 28 days
	Schnitzler syndrome		

Coding:

HCPCS Code	Description
J0638	Injection, canakinumab, 1 billable unit = 1 mg
J2793	Injection, rilonacept, 1 billable unit = 1 mg

Background:

Cryopyrin-Associated Periodic Syndromes (CAPS)

Cryopyrin-associated periodic syndromes are auto inflammatory disorders associated with a defect in the IL-1 pathway. These syndromes are uniformly characterized by a pathogenic variant in a single gene, *NLRP3.* CAPS has multiple phenotypic differences which can present as Familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), Neonatal-onset multisystem inflammatory disease (NOMID), and Chronic infantile neurologic cutaneous and articular (CINCA) syndrome. Treatment of CAPS consists of agents that target the IL-1 pathway. Both anakinra (Kineret) and rilonacept (Arcalyst) are FDA approved for the treatment of CAPS. The clinical trials for these agents observed a positive response in disease specific symptoms and inflammatory markers.

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.

Systemic Juvenile Idiopathic Arthritis (SJIA)

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 2021 American College of Rheumatology (ACR) guidelines on SJIA conditionally recommend NSAIDS as first line monotherapy. The lowest effective dose and shortest duration of glucocorticoids is conditionally recommended when biological DMARDs are not immediately available.

Adult Onset Still's Disease (AOSD)

Adult Onset Still's disease (AOSD) is an inflammatory disorder characterized by daily fevers, arthritis, and an evanescent rash. AOSD and sJIA are increasingly recognized to fall on the same clinical continuum, and AOSD is the term most widely used when the condition begins after age 16. AOSD can be associated with macrophage activation syndrome (MAS) which is a hyperinflammatory state characterized by fever, hepatosplenomegaly, and multiple lab abnormalities. MAS is a serious but rare manifestation of AOSD. Per UpToDate, NSAIDs are considered first line therapy followed by glucocorticoids if insufficient. IL-1 and IL-6 inhibition have been identified as appropriate treatment targets for this disease. Canakinumab (Ilaris) is FDA approved for AOSD and its approval was based on extrapolation of safety and efficacy data in patients with SJIA.

Tumor Necrosis Factor Receptor Associated Periodic Syndromes (TRAPS)

Tumor necrosis factor (TNF) receptor associated periodic syndrome (TRAPS) is a rare genetic disorder that affects approximately one person per million. TRAPS diagnosis is confirmed by TNFRSF1A genetic mutation in addition to prolonged fevers lasting 5 or more days and one additional clinical hallmark feature, such as myalgias, limb pain, abdominal symptoms (pain, vomiting), rash, headache, lymphadenopathy, chest pain, conjunctivitis, or periorbital edema. Patients with three or more flares per year with inadequate response to oral glucocorticoids may be treated with prophylactic therapy with monoclonal antibodies that block IL-receptors. The 2021 European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACR) Guidelines for Treatment of Interleukin-1 Mediated Autoinflammatory Disease recognize both canakinumab (Ilaris) and anakinra (Kineret) as potential treatment options for prophylaxis over DMARDs.

Familial Mediterranean Fever (FMF)

Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disorder characterized by recurrent bouts of fever lasting a couple of days and serosal inflammation (e.g., peritonitis, pleuritis, pericarditis, synovitis) or erysipelas-like-erythema. Untreated FMF may lead to the development of secondary amyloidosis with eventual renal failure. The 2016 EULAR Recommendations for the Management of Familial Mediterranean Fever recommends colchicine as first line therapy and notes colchicine should be started as soon as a clinical diagnosis is made (grade A recommendation). The guidelines note that IL-1 blockers may be a treatment option based on case reports demonstrating successful use of anakinra (Kineret).

Hyperimmunoglobulin D Syndrome/Mevalonate Kinase Deficiency (HIDS/MKD)

Mevalonate Kinase Deficiency (MKD), formerly called Hyperimmunoglobulin D Syndrome (HIDS), is a rare, autosomal-recessive genetic disorder. Classic HIDS is due to compound heterozygous or homozygous V3771 mutation in the mevalonate kinase (MVK) gene. HIDS/MKD is characterized by recurrent febrile episodes lasting four or more days with chills and lymphadenopathy, abdominal pain, and elevated serum IgD levels above 14 mg/mL. Over 90% of patients have palpable lymphadenopathy during a febrile episode and 85% of patients present with abdominal pain (with or without vomiting and diarrhea). Elevated IgD levels are considered to be a secondary effect to the inflammatory process and patients may not always present with an elevated IgD level. In such cases, genetic testing of V3771 mutation may be completed to confirm diagnosis. The 2021 EULAR and ACR Guidelines for Treatment of Interleukin-1 Mediated Autoinflammatory Diseases recommend treatment with IL-1 antagonist as first line therapy for HIDS/MKD prophylaxis (grade C recommendation).

Recurrent Pericarditis

Both the European Society of Cardiology (ESC) and American College of Cardiology (ACC) review on management of acute and recurrent pericarditis list treatment with NSAIDs/aspirin and colchicine as treatment options. Low-dose corticosteroids are also often used in the treatment of recurrent pericarditis and are associated with high treatment success rate per ACC. Rilonacept (Arcalyst) is FDA approved for the treatment of recurrent pericarditis and reduction in risk recurrence in adults and children 12 years of age and older. Currently, the place in therapy for rilonacept (Arcalyst) can be considered for patients with multiple recurrence of pericarditis, and/or for patients where further use of NSAIDs, colchicine, and a low-dose corticosteroid are not clinically appropriate.

Gout Flare

A gout flare is intensely painful and disabling which typically affects a single joint, although flares affecting multiple joints may occur. Per the American College of Rheumatology (ACR) guidelines on gout, colchicine, NSAIDs, or glucocorticoids are strongly recommended as appropriate first line therapy over IL-1 inhibitors or ACTH. Guidelines define frequent flares as $\geq$ 2 annually. For patients who poorly tolerate or are contraindicated to these therapies, IL-1 inhibitors are indicated. Canakinumab (Ilaris) is FDA approved and indicated for treatment of acute gout flares.

Deficiency of IL-1 Receptor Antagonist (DIRA)

Deficiency of IL-1 receptor antagonist (DIRA) is an autosomal recessive disorder due to a pathogenic variant in *IL1RN* which encodes the IL-1 receptor antagonist. This rare condition presents in early infancy and is characterized by a diffuse pustular skin rash, sterile osteomyelitis, and nail changes. The 2021 EULAR/ACR recommendations for DIRA recommend treatment with IL-1 blockers, including anakinra and rilonacept, which have shown benefit in controlling disease flares and in preventing long term complications.

Schnitzler Syndrome

Schnitzler syndrome is a rare inflammatory disorder characterized by a chronic urticaria-like rash and IgM monoclonal gammopathy. The disease may also be accompanied by other systemic symptoms such as fever, bone and muscle pain. The safety and efficacy of anakinra was demonstrated in an observational study where complete remission was achieved in 83% of patients and the remaining 17% achieved a partial response.

References:

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History:

Approved Date	Effective Date	Version	Action and Summary of Changes
08.14.2024	04.01.2025	66.27.00.AI-5	- Updated language for adalimumab biosimilars - Formatting updates
08.14.2024	03.01.2025	66.27.00.AI-4	Approved by DUR Board - Split 66.27.00 policy into different policies -Added new drug indications when applicable -Update language in medical necessity section

Previous policy changes (relevant from Cytokine & CAM Antagonists Policy)	
Date	**Action and Summary of Changes**
10.21.2021	Removed Hyrimoz from the policy and updated the initial dosing for infliximab.
11.30.2020	Removed Preferred/Non-Preferred listing and added link to AHPDL publication
11.12.2020	Added language in clinical policy section for cases which do not meet policy criteria
09.01.2020	Updated wording in clinical criteria for products with only one preferred option.
08.19.2020	Approved by DUR Board
8.20.2020	Update to dosing and limits section for all products and indications
08.12.2020	Updated policy clinical criteria and dosing & quantity limits to include nonradiographic axial spondyloarthritis
06.01.2020	Added new agents to class; updated age limit for Uveitis indication; updated dosing and quantity limits; updated HCPCS coding
07.31.2019	Updated criteria that trial of preferred biologics only applies to non-preferred biologics
06.07.2019	Updates to TB skin test requirements for apremalist; updates to initial authorization clinical criteria
11.02.2018	Addition of Hyrimoz (adalimumab-adaz)
09.07.2018	Addition of new medication
08.16.2017	New Policy